X. MULTIDISCIPLINARY CANCER RESEARCH CONGRESS

ABSTRACT BOOK

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MOKAD

MOLEKÜLER KANSER ARAŞTIRMA DERNEĞİ

08-11 MAY 2025

ESKİŞEHİR, TÜRKİYE

Questa Thermal & Spa Hotel

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EACR
European Association for Cancer Research

ISU ISTINYE UNIVERSITY ISTANBUL

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https://sites.google.com/view/10thmokadcongress

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About Registration, Awards, Bursary Applications & General Issues

Yaren Arasan

About Sponsorship

Ecem Esma Yeğin

Remzi Okan Akar

Dear Cancer Researchers,

As Molecular Cancer Research Association (**MOKAD**), we are excited to announce that MOKAD 2025 Congress (X. Multidisciplinary Cancer Research Congress) is on the way. The congress will be held on **May 8-11, 2025** at **Questa Thermal & Spa Hotel** in **Eskişehir**.

At the 2025 Eskişehir MOKAD congress, **we will be breaking new grounds**: Posters will exceptionally be valued. There will be **poster sessions that discuss and educate**. A format is planned where posters in the same thematic area are gathered around the relevant round table, a competent researcher of the subject is at the head, the poster is presented in detail, the poster is discussed by the participants of that theme, questions are asked, and if necessary, training is provided. We hope that the congress will be rich in poster sessions. Another first of the congress is that the three best posters will receive **an award certificate to be documented directly by the EACR Headquarter**. In addition, MOKAD will also award prizes to the three best oral presentations. Some plenary lectures, satellite symposiums/sponsor presentations and short talks will also take place. In summary, this bilingual MOKAD congress will be a special congress with a different format of poster session. As usual, the maximum number of "**Young Researcher Scholarships**" will be provided with the support of the association/MOKAD. Classic MOKAD awards will also be presented. The language of the congress will be English and Turkish.

The main thematic areas of the congress are expected to be "*Cancer Bioinformatics, Epigenetics and Cancer, Long noncoding RNA and Death/Life, Viability/Cytotoxicity Analysis, Anticancer Drug Development, Tumor Biology and Metastasis, CTC and Precision Oncology, Cancer Stem Cells and Microenvironment, Spheroid/Organoid, New Technologies for Therapeutic Purposes*".

The scientific intensity of the congress will be balanced with an extended social program exploring the natural and cultural richness of Eskişehir. In addition, the thermal water pool and spa center of Questa Hotel (https://questahotel.com/questa-eskisehir.html), which participants will benefit from free of charge, will be a bonus.

MOKAD looks forward to keeping you up to date in cancer research and welcoming you in Eskisehir in advance…

On behalf of Congress Organization and MOKAD Board of Directors

Engin ULUKAYA

Değerli Kanser Araştırmacıları,

Moleküler Kanser Araştırma Derneği (**MOKAD**) olarak, 2025 yılı Kongremizi (X. Multidisciplinary Cancer Research Congress) hazırlamanın heyecanı içindeyiz. Kongremiz, **8-11 Mayıs 2025** tarihlerinde **Eskişehir**'de **Questa Thermal & Spa Hotelde** düzenlenecektir.

2025 Eskişehir kongresinde **bazı ilklere imza atıyor** olacağız: Posterler ulusal veya uluslararası hiçbir kongrede olmadığı kadar büyük değer görecektir. **Tartışan ve eğiten poster oturumları** olacaktır. Aynı tematik alandaki posterlerin ilgili yuvarlak masa etrafında toplandığı, başında konunun yetkin bir isminin olduğu, posterin detaylı sunulduğu, o temaya katılanlar tarafından tartışıldığı, sorular sorulduğu, gerekirse eğitim verildiği bir format planlanmıştır. Bu yüzden, poster ağırlıklı bir kongre olmasını diliyoruz. Kongrenin bir başka ilki, en iyi üç postere doğrudan **EACR tarafından belgelenmek üzere ödül sertifikası** verilecek olmasıdır. MOKAD tarafından da en iyi üç sözlü sunuma ödül verilecektir. Ayrıca, konferanslar, uydu sempozyumları/firma sunumları ve kısa konuşmalar da yer alacaktır. Özetle, iki dilde düzenlenen MOKAD kongresi farklı formatıyla özel bir kongre olacaktır. Gene her zamanki gibi, derneğin desteğiyle maksimum sayıda "**Genç Araştırmacı Bursu**" sağlanacaktır. Klasik MOKAD ödülleri de gene sahibini bulacaktır. Kongre dili İngilizce ve Türkçe olacaktır.

Kongrenin tematik alanlarının "*Kanser Biyoinformatiği, Epigenetik ve Kanser, Long noncoding RNA ve Ölüm/Yaşam, Canlılık/Sitotoksisite Analizleri, Antikanser İlaç Geliştirme, Tümör Biyolojisi ve Metastaz, CTC ve Hassas Onkoloji, Kanser Kök Hücre ve Mikroçevre, Sferoid/Organoid, Tedavi Amaçlı Yeni Teknolojiler*" konularından oluşacağı beklenmektedir.

Kongrenin bilimsel yoğunluğu Eskişehir'in doğal ve kültürel zenginliklerinin keşfedildiği uzun süreli bir sosyal programla dengelenecektir. Ayrıca, katılımcıların ücretsiz yararlanacağı Questa Hotel'in (https://questahotel.com/questa-eskisehir.html) termal sulu havuz ve spa merkezi de bonus olacaktır.

MOKAD, Eskişehir'de kanser araştırmada günceli yakalamayı ve sizleri ağırlamayı sabırsızlıkla bekliyor…

Kongre Düzenleme ve MOKAD Yönetim Kurulu Adına

Engin ULUKAYA

Congress Program

8TH MAY 2025

13:00 - 15:00	**COURSE** **Engin Ulukaya** Canlılık/Sitotoksisite ve İlaç Geliştirmede Kritik Konular (Ücretsiz Kurs)
15:00 - 15:30	**OPENING CEREMONY**
15:30 - 16:10	**OPENING LECTURE** **Chair: Engin Ulukaya** **Mazhar Adlı (USA)** How to functionally characterize all human genes
16:10 - 16:40	**PLENARY LECTURE 1** **Chair: Konstantinos Dimas** **Ömer Faruk Bayrak** Importance of tumor typing for cancer patients and future perspectives of molecular biology of cancer
16:40 - 17:10	**PLENARY LECTURE 2** **Chair: Ömer Faruk Bayrak** **Konstantinos Dimas (GREECE)** Mouse Models and Critical Considerations in Anticancer Drug Development *Sponsored Speaker* EACR European Association for Cancer Research
17:10 - 17:30	**PLENARY LECTURE 3** **Chair: İlhan Yaylım** **Selin Ulukaya (GERMANY)** Single Cell Proteomics
18:30 – 19:30	**OPENING COCKTAIL** *(At the Congress Hotel)*

<table>
<tr><th colspan="3">9TH MAY 2025</th></tr>
<tr><td>9:00 - 11:00</td><td>PANEL 1
Chairs: Cihan Taştan & Egemen Dere
Cell Therapies and Tumor Microenvironment
<u>Cihan Taştan</u> – The Role of CAR-T Cell Memory Profile in Hematological Cancers: Pre-Clinical Perspectives
<u>Raife Dilek Turan</u> – Yeni Nesil CAR-T Hücre Terapileri: Klinik Uygulamalardaki Gelecek Perspektifleri
<u>Didem Karakaş Zeybek</u> – Nerve-Cancer Crosstalk: A Hidden Dimension Driving Pancreatic Cancer Aggressiveness
<u>Aslı Kutlu</u> – Evaluation of the potential role(s) of small molecules in overcoming temozolomide resistance in glioblastoma multiforme: wet lab and in-silico studies</td><td>ORAL PRESENTATIONS
Chairs: Abdullah Yalçın & Nilgün Demir
Natural Products & Cancer
Fatih Kar
Reyhan Tahtasakal
Hacer Kaya Çakır
Aysun İnan Genç
Aslıhan Şengelen
Yunus Aksüt
Merve Göztepe
Gülçin Özkara
Tumor Biology
Esra Nalbat
Muhlis Akman
Senem Noyan
Ali Utku Turhan
Ceren Sumer
Ceyda Çolakoğlu Bergel</td></tr>
<tr><td>11:00 - 11:30</td><td colspan="2">Coffee Break</td></tr>
<tr><td>11:30 - 12:30</td><td>PANEL 2
Chairs: Tuba Günel & Bünyamin Akgül
Personalized Oncology and Cell Death
<u>Tuba Günel</u> – Personalized Medicine Approach using Lateral Flow Based Diagnostic Kit in Ovarian Cancer Screening
<u>Abdullah Yalçın</u> – Modulation of sensitivity to ferroptosis by PFKFB proteins in cancer cells
<u>Orçun Can</u> – Akciğer Kanserinde Kişiselleştirilmiş Onkoloji</td><td rowspan="2">ORAL PRESENTATIONS
Chairs: Serdar Karakurt & Pınar Siyah
Chemotherapeutics & Cancer
Egemen Dere
Vildan Betül Yenigün
Ebru Nur Dursun
Sude Eris
Serra Sener
İlknur Yıldız & Aseel Sadıq Mohammed Khamis
Ceyda Çolakoğlu Bergel
Sinan Tetikoğlu
İbrahim Bayav</td></tr>
<tr><td>12:30 - 13:00</td><td>SATELLITE SYMPOSIUM
<u>Medsantek</u></td></tr>
</table>

13:00 - 14:00	***Break***
14:00 - 16:00	**INNOVATIVE POSTER SESSION**

Tumor Biology	Tumor Biology 2	Tumor Biology & Chemotherapeutics	Natural Products & Cancer	Natural Products & Nanotechnology	Novel Technologies	Chemotherapeutics & Cancer
Mazhar Adlı & Muhlis Akman	**Bünyamin Akgül & Zelal Adıgüzel**	**Serdar Karakurt & Merve Erkısa Genel**	**Serap Çelikler & Ömer Faruk Bayrak**	**Ayşegül Çebi & Mehtap Kutlu**	**Aslı Kutlu & Zuhal Hamurcu**	**Gamze Tanrıöver & Didem Karakaş Zeybek**
1. Gökçe Güllü Amuran: Urinary Crk Concentration Analysis For The Prediction Of Recurrence In Non Muscle Invasive Bladder	**1. Yaren Durusoy:** Impact Of Glutamine Utilization Through Tricarboxylic Acid Cycle On Lipid Metabolism İn Sw480 And Sw620 Cells	**1. Semra Demokan:** Investigation Of Methylation-Related Expression Changes Of Gabrb3 Gene İn Oral Malignant Lesions	**1. Sude Kocabıyık:** Apoptotic Molecular Mechanism Of Protein-Rich Macrovipera Lebetinus Snake Venom İn Colorectal Cancer Cells İn Turkiye	**1. Cagla Ozdenizer:** Differential Cross-Talk Of Staphylococcus Epidermidis İn A Co-Culture Model Of Lung Cancer And Bronchial Epithelial Cells	**1. Gamze Usaç:** Re-Evaluation Of Personally Appropriate Therapeutic Approaches İn Patients Diagnosed With Small Cell Lung Cancer With Liquid Biopsy And Clinical Data Integration	**1. İrem Bayram & Sude Kale:** 2b Ve 3b İn Vitro Kültür Ortamında Farklı Stratejiler Ile Geliştirilen Gemcitabin Direnç Mekanizmasının Kolanjiyokarsinoma Hücre Hatları Özelinde Araştırılması
2. Aybike Sarıoğlu Bozkurt: Dual Inhibition Of Pfkfb3 And Odc1 Exhibits Enhanced Antiproliferative Effect On Pancreatic Cancer Cells	**2. Mahinur Basci:** Investigation Of The Effects Of Zrf1 Protein On Neutrophil Chemotaxis And Polarization Via Paracrine Signaling İn Breast Cancer	**2. Semra Demokan:** Investigation Of Methylation And Expression Levels İn Stk32c Gene İn Oral Malignant Lesions	**2. Irem Mukaddes Bılgıseven:** Activation Of Apoptotic Pathways İn Colon Cancer Cells: Effects Of Apis Mellifera Anatoliaca Venom At The Gene And Protein Levels	**2. Uygar Alaman:** Effect Of Different Serum Concentrations On Breast Cancer Cells İnfected With Staphylococcus Spp.	**2. Mehmet Katıpoglu:** May The Newly Identified Interleukins Be Considered As A New Potential Therapeutic Target In The Treatment Of Breast Cancer?	**2. Abdulmelik Aytatlı:** Salinomycin Overcomes Taxol-Resistance İn Head And Neck Cancer Cells By Inhibiting Viability, Clonogenic Potential And Migration
3. Nazlıcan Sıla Akkaş: Characterization Of A Novel Intronic Rna İn Breast Cancer And Its Possible Interactions With Micrornas	**3.Büşra Ertunç:** Determination Of The Effect Of Nutrient Limitation On P-Glycoprotein Expression And On Pathways Controlling P-Gp Expression: Possible Chemosensitization Via Verapamil Treatment	**3.Madina Alıyeva:** Tiroid Kanseri Hücre Hatlarında Circptpn22'nin Ekspresyonunun Araştırılması	**3. Nilay Tufan:** Investigation Of The Antioxidant Analyses Of Anatolian Saffron And Its Cytotoxic Effects On Prostate Cancer Cells	**3. Onur Onguncan:** Resveratrol Enhances The Antiproliferative Effect Of Glut-1 Inhibition İn Lung Cancer Models	**3. Kubra Temiz:** Importazole As A Novel İnhibitor Of Arf6: Inhibits The Growth Of Colon Cells And İnduces Apoptosis	**3. Ceren Sumer:** Combined Effects Of Ranolazine And A Tyrosine Kinase İnhibitor (Ag1478) On Breast Cancer Cell Invasiveness
4. Nesrin Dinc: Investigating The Effects Of Long Non-Coding Rnas İn Triple Negative Breast Cancer Pathogenesis	**4. Gamze Yılmaz:** Effects Of Mir-155-5p On Migration And Autophagy İn Lung Cancer Cells	**4. Tolga Coşkun:** Staphylococcus Epidermidis İle Enfekte Edilmiş Keratinosit Hücre Hattı Ve Melanom Deri Kanseri Hücrelerinde Ultraviyole Işınların Kanserojen Etkileri	**4. Fatıma Zehra Yılmaz:** Investigation Of The Anti-Cancer Effects Of Stypopodium Schimperii And Its Potential For Commercial Use	**4. Tuğbağ Bayram:** Gst Activities Of Ornithogalum Sigmoideum On Hepg2 Hepatocellular Carcinoma And Ht-29 Colon Cancer Cell Lines	**4. Özlem Biçen Ünlüer:** Novel Heteroleptic Iridium (Iii) Complex For Bioimaging Of Lung Cancer Cells	**4. Oner Sonmez:** Synergistic Antiproliferative Effect Of Fx-11 And Benztropine Combination Via Emt Modulation İn Pancreatic Cancer Cells
5. Neslisah Barlak: Investigating The Role Of Fucosyltransferase Genes On Cancer Stem Cell Potential-Associated Phenotypes İn Head And Neck Squamous Cell Carcinoma	**5. Tutku Güler:** Olfactory Receptor Or2a4/7 And Its Effects On Epithelial-Mesenchymal Plasticity İn Colorectal Cancer	**5. Taner Kasapoglu:** Tumor-Associated Schwann Cells Decreased Natural Killer Cell Activity Against Pancreatic Cancer Cells	**5. Elif Bozkır:** Pro-Apoptotic And Oncogene-Suppressing Effects Of Stypopodium Schimperii Extracts On Human Colorectal Carcinoma	**5. Zeynep Özman Gökçe:** Immunomodulatory Effects Of Walnut Husk Extract On Lps-Stimulated Raw 264.7 Cells And Its Cytotoxic Impact On K7m2 Osteosarcoma Cells	**5. Ufuk Mert:** Akciğer Kanseri Hastalarının Ardışık Tükürük Ve Dışkı Örneklerinde Bakteriyel Ve Ökaryotik Mikrobiyota İle Lipidomik Verilerin Entegrasyonu	**5. Ahsenur Sevim:** Dubermatinib May Enhance The Anti-Cancer Efficacy Of Gemcitabine On Panc-1 Cells
6. Zeynep Akçin: Identification Of The 3' Utr Mutations Of The Il7r Gene İn Lung Cancer, Breast Cancer, And Melanoma	**6. Elif Bayram:** A Novel Antiproliferative Strategy: Synergistic Inhibition Of Cancer Cell Viability Via Got1 Targeting And Cepharanthine	**6. Cansu Yaren Kelkitli:** Temozolomid Dirençli (T98g) Ve Duyarlı (U87) Glioblastoma Multiforme Hücre Hatlarında Direnç Gelişim Sürecinin 2b İn Vitro Kültür Ortamında Ozmotik Basınç Değişiklikleri Ve Ortamdaki Seçilmiş Elementlerin Rolü Açısından İncelenmesi	**6. Nilay Sarıbaş:** Resveratrol-İnduced Cytotoxicity İn Colorectal Cancer: Influence Of Microsatellite Stability	**6. Ebru Kanimdan:** Dual Impact Of A Herbal Oil Combination On Sars-Cov-2 Entry Pathways And Tumorigenic Signaling İn Colon Adenocarcinoma Cells	**6. Zeynep Çelik:** Pankreas Kanseri Araştırmalarında İdeal 3d Sferoid Modellerin Belirlenmesi: Agaroz Ve Gelma'nın Karşılaştırılması	**6. İlayda İncekara:** An Already Prescribed Antidepressant, Vortioxetine, Can Be Considered As A Trustworthy Partner Of A Novel Combinatorial Therapy For Ovarian Cancer Patients
7. Unal Arabacı: Evaluating Bd1008 As A Promising Therapeutic Candidate İn Glioblastoma Treatment	**7. Gamze Turan:** Exploring Esr1 And Its Transcriptional Network İn Luminal Breast Cancer	**7. Vera Avcı:** Investigation Of Autophagy-Associated Vps34 Inhibitor Via Wnt/B-Catenin Signaling Pathway İn Pancreatic Cancer Cell Line	**7. Elif Bekmezci:** Effects Of Iurus Kinzelbachi Scorpion Venom On Mtor And Mapk Pathways In Human Colorectal Carcinoma	**7. Ece Oylumlu:** Glioblastoma Hücrelerinin Anjiyogenezinde Etkin Rol Oynadığı Bilinen Vegfr Sinyal Yolağı, Yeni Bir İnhibitör Olan Donafenib Ile Baskılanabilir Mi?	**7. Tunc Unal:** Crıspr Base Editing Mediated Fluorescent Signal Disruption On Monogenic Hek293t Cells	**7. Aisha Rasulova:** Kemoterapi Dirençli Akciğer Kanseri Hücrelerinde Fingolimodun Sitotoksik Ve Proapoptotik Etkileri
8. Miray Sevinin: Unraveling The Role Of Tap73β İn Hepatocellular Carcinoma By Driving Metastasis, Angiogenesis, And Sorafenib Resistance İn The Zebrafish Xenograft Model	**8. Nevruz Alis Soyleyici:** Effects Of Dual Targeting Of Malic Enzyme And Nrf2 On Cell Viability And Redox Balance İn A549 Cells	**8. Ceren Sarı:** Meme Kanseri Hücreleri Lipoprotein İçermeyen Ortamda Aerobik Glikolizi Baskılar	**8. Ece Vardar:** Taraxacum Officinale Ve Leontice Leontopetalum L. Ekstrelerinin Antioksidan Ve Sitotoksik Aktiviteleri	**8. İlkem Turnalı Önsoy:** Investigation Of The Synergistic Effect Of Quercetin And Epigallocatechin Gallate On Doxorubicin İn Triple Negative Breast Cancer Cell Lines	**8. Furkan Turan:** Therapeutic Effects Of The Antihistamine Desloratadine İn Head And Neck Squamous Cell Carcinoma	**8. İlayda Polat:** İnsan Somatik Hibrit Hücrelerinde Bevacizumab Ve Carmofurun Hücre Canlılığına Etkileri
9. Emir Çelik: Investigation Of The Differential Effects Of L-Glutamine Starvation On Lipid Droplet Formation And Migration Capacity Of Colorectal Cancer Cells Sw480 And Sw620	**9. Özge Deniz Yeşil Baysal:** Deciphering The Role Of Purine Metabolic Enzymes İn Ovarian Cancer	**9. Nilay Dinckurt:** Epidermal Growth Factor And Androgen Receptors Dual Targeting By Osimertinib And Enzalutamide Reversed Epithelial-Mesenchymal Transition And İnduced Apoptosis İn Glioblastoma Cell Lines	**9. Işıl Özdemir:** Investigation Of The Eurects Of Zinc-Borate Treatment On The Lipid Metabolism Of Sw480 And Sw620 Colorectal Cancer Cells	**9. Berin Skenderi:** Green Synthesis Of Zinc Oxide Nanoparticles (Znonps) And Investigation Of Their Cytotoxic Effects On Colorectal Carcinoma Cells	**9. Funda Kosova:** Effects Of Biomarkers On Cancer Invasion İn Patients With Prostate Cancer	**9. Ayşe Keskin Günay:** Modulation Of Angiogenic Activity With 24-Epibrassinolide And/Or Temozolomide Treatment İn Huvec Cells
	10.Leila Sabour Takanlou: EZH2 İnhibitor Tazemetostat Effect on Apoptosis and WNT Signaling Pathway in Anaplastic Thyroid Cancer Cells	**10. Ezgi Karyemez:** Targeting Nnmt To Overcome Taxane Resistance İn Castration-Resistant Prostate Cancer	**10. Ecesu Atmaca:** Natural Compounds İn Cancer Therapy: The Role Of Curcumin And Bromelain İn Triple-Negative Breast Cancer		**10. Gizem Bulut:** A Palladium Complex {[Pd(Bpma)(Barb)Cl]·H 2 O} Triggers Oxidative Stress-Mediated Apoptosis On Ovarian Cancer Cell Lines	**10. Sendegul Yildirim:** Investigation Of The Effects Of Tas-115 On A 3d Triple Negative Breast Cancer Model
		11. Merve Erkısa Genel: Palladium(Ii)-Barbiturate Complex: A Promising Treatment Options For Braf-Mutant Colorectal Cancer	**11. Deniz Ece:** Staphylococcus Aureus Enfeksiyonunun Akciğer Kanseri Ve Normal Bronşiyal Hücreler Üzerindeki Farklı Etkileri		**11. Fatma Ortabakan:** Hydrocephalus Microenvironment; A Revolutionary Era İn The Diagnosis Of Brain Tumors	
			12. Serdar Karakurt: The Impact Of Scorpion Venom On Autophagy: A Double-Edged Sword İn Cancer Therapy		**12. Merve İnel:** Fluorescent Warriors: Design And Evaluation Of Novel Isatin-Based Compounds As Dual-Action Agents Against Breast Cancer	

16:00 - 16:30	***Coffee Break***	
16:30 - 17:30	**PANEL 3** **Chairs: Orçun Can & Serpil Oğuztüzün** **Novel Technologies in Cancer Treatment** **Damian Bell (UK) –** *Cancer and Ion Channels* **Murat Köylü –** *Elektrik alan terapisi: Kanser tedavisinde yeni bir modalite* **Figen Celep Eyüboğlu –** *3D Organoid Kültürler ve Kanserde Kullanım Alanları*	**ORAL PRESENTATIONS** **Chairs: Berkcan Doğan & Merve Erkısa Genel** **Novel Technologies** Gamze Nur Öter Aslı Semerci Ece Vardar Zehra Elif Günyüz Nevin Belder Asuman Çelebi

10TH MAY 2025		
9:00 – 9:20	**PLENARY LECTURE 4** **Chair: Serap Çelikler** **Gamze Tanrıöver** GBM'de Meydan Okumak: Zihnin Sınırlarında Yenilikçi Tedavi Stratejilerinin Peşinde	**ORAL PRESENTATIONS** **Chairs: Didem Karakaş Zeybek & Yeliz Sahilli** **Tumor Biology** Fatih Kar Elif Apaydın Ece Gümüşoğlu Acar Medi Kori Seçil Eroğlu Bilgi Erbay Berkcan Doğan Leyla Tutar
9:20 – 11:00	**SHORT TALKS** **Chairs: Şehime Temel & Işık Didem Karagöz** Pınar Siyah Nurettin İlter Sever İrem Durmaz Şahin Mehmet Sarımahmut	**Natural Products & Cancer** Melisa Tecik Elif Beyza Koç Asuman Çelebi Venhar Çınar Sare Uyurca
11:00 - 11:30	***Coffee Break***	
11:30 – 13:00	**SHORT TALKS** Emel Sokullu	**ORAL PRESENTATIONS** **Chairs: Yağmur Kiraz &**

	Sedef Ziyanok Demirtaş Didem Seven Gökhan Görgişen Elif Uz Yıldırım	**Mehmet Sarımahmut** **Natural Products & Cancer** Işık Didem Karagöz Gamze Yılmaz Esin Güvenir Çelik Gamze Kuzkun İlkem Tunali Önsoy **Nanotechnology & Cancer** Ehed Muhammed Aymaz Pınar Elife Doğan Kemal Baş
13:00 – 14:00	**ÇALIŞTAY** **Hüseyin Köse & Bahar Demir** Kadınlarda Öz Savunma	
14:00 – 18:00	**SOCIAL PROGRAM** *Odunpazarı & Sazova Park*	
20:00 – 24:00	**GALA DINNER** *(At the Congress Hotel)*	

11TH MAY 2025	
9:00 - 11:10	**ORAL PRESENTATIONS** **Chairs: Didem Seven & Muhlis Akman** **Tumor Biology** Tuba Denkçeken Elif Onur Gamze Turan Nazife Ege Gülfırat Buse Akdemir Ebru Kırmızıay Nazlıcan Kaygusuz Gizel Gerdan Eren Son Demet Kaçaroğlu
11:10 - 11:30	***Coffee Break***

11:30 – 13:00	**PANEL 3** **Chairs: Semra Demokan & Huri Demirci** **Anticancer Drug Development** **Huri Demirci –** *The Critical Role of Structural Biology Studies in Preclinical Targeted Drug Development* **Arif Kıvrak –** *Synthesis and Cytotoxicity Evaluation of Novel Endoperoxide Derivatives as Potential Anti-Cancer Agents* **Ayşegül Çebi –** *Anticancer Agents from Natural Products* **Yağmur Kiraz –** *Novel Approaches to Leukemia Treatments and Drug Repurposing Strategies*	**Chairs: Sedef Ziyanok & Aslı Kutlu** **ORAL PRESENTATIONS** **Cell Death & Cancer** Ece Oylumlu Kübra Nur Kaplan İlhan Begüm Akyürek Fatma Seçer Çelik Erva Özkan Zübeyir Elmazoğlu Aliye Ezgi Güleç Taşkıran Zeynep Tıraşoğlu Senanur Aslan Fatma Akat Eissa Almaghrebi
13:00 - 13:40	**CLOSING LECTURE** **Chair: Ayşegül Çebi** **Bünyamin Akgül** Long non-coding RNAs in cell death and survival	
	CLOSING & AWARD CEREMONY	

Kurs

Sitotoksisite ve Hücre Ölümü Yöntemlerinin Değerlendirmelerinde Kritik Konular

Engin Ulukaya
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In vitro (preklinik) sitotoksisite testleri ilaç geliştirmedeki ilk aşamalardan biridir. Özellikle kanser ilaçlarının keşfinde ve geliştirilmesinde çok önemli yer tutarlar. Önemi, bu aşamanın doğru yapılıp yapılmaması ardından gelecek aşamaların maliyetini, dolayısıyla ilaç geliştirmedeki toplam harcama yükünü, doğrudan etkilemesinden kaynaklanmaktadır. Bu testlerin sonucuna göre yeni ilaçlar ilk değerlendirmeyi geçtikleri takdirde, hayvan deneyleri ve ardından klinik çalışmalara (Faz I-III çalışmalarına) ilerlerler. İn vitro sitotoksisite testleri ilk aşama olduğundan, bu aşamada yanlış seçilen ve/veya değerlendirilen testler bir sonraki aşamalarda ciddi maliyet sorunlarına ve zaman kayıplarına yol açabilirler. Bu nedenle, bu testlerin seçimi ve sonuçların doğru değerlendirilmesi önemlidir. Doğru seçim ve değerlendirmeyi etkileyen birçok faktör bulunmaktadır: a) testlerin ölçebildikleri en az canlı hücre sayısı, b) testlerin olası interferansları, c) testlerin son-nokta ölüm testi veya proliferasyon testi olup olmaması, d) testlerin metabolik aktivite ile ilişkisi, e) veri kalitesi, f) dinamik aralığı, g) kolay ve hızlı kullanımı, h) ayraçlarının stabilitesi, i) maliyet-etkinlik durumu, j) hücre membranı bütünlüğü ile ilişkisi, h) hücreden hücreye değişebilen optimum test çeşidi vs. Tüm bu faktörler test seçimi ve sağlıklı değerlendirme için göz önünde bulundurulmalıdır. Test ayraçlarının kullanılan ajanlarla interferans olasılıkları veya pH değişiklikleri özellikle MTT testi gibi metodlarla çalışanların dikkat etmesi gereken problemlerdir. Çünkü bu faktörler MTT sonuçlarının yanlış yorumlanmasına yol açmaktadırlar. Ya da, hücreler öldüğü halde, canlılık varmış gibi sonuç alınabilir. Bu durum, bitki ekstraktlarını MTT testi ile çalışırken sık rastlanan bir problemdir. ATP testi, luminesans teknolojiyle çalışması açısından kolorimetrik veya florometrik yöntemlere göre daha sensitif bir yöntemdir. Bu metot ile daha az sayıda canlı hücre kantite edilebilir. Fakat, bu yöntemi de dikkatli kullanmak gerekir çünkü hücre ölümüne yol açmadan ATP inhibe edici ajanlarla çalışıyor olunabilir. Primer (ex vivo) kültürlerde özellikle kanser hücresi dışındaki normal hücrelerin sitotoksik ajana yanıtları da dikkate alınmalıdır. Bu yüzden, primer kültürlerdeki sitotoksisite ölçümleri esnasında normal hücreler ortamdan olabildiğince temizlenmelidir. Aksi takdirde, elde edilen sitotoksik etki sadece malign hücrelerin değil aynı zamanda normal hücrelerin de yanıtı olarak karşımıza çıkabilir. Sonuç olarak, sitotoksisite testlerinin çalışma prensipleri ve olası sorunları göz önünde bulundurularak, ayrıca test edilecek ajanın özelliğine ve hücre türüne göre optimum test seçimi değişebilir. Bu konuşmada özellikle pratikte karşımıza çıkan bazı önemli faktörler örneklerle anlatılacaktır.

1. Ulukaya E, Colakogullari M and Wood E J. Interference by anti-cancer chemotherapeutic agents in the MTT - tumor chemosensitivity assay. *Chemotherapy* 50:43-50, 2004

2. Ulukaya E, Ozdikicioglu F, Yilmaztepe A et al. The MTT assay yields a relatively lower result of growth inhibition than the ATP assay depending on the chemotherapeutic drugs tested. *Toxicol In Vitro.* 22(1):232-9, 2008

3. Ari F, İkitimur EI, Ulukaya E. The ATP assay, but not the MTT assay, detects further cytotoxicity of the combination of anthracyline-based therapy with histone deacetylase inhibitor (Valproic acid) in breast cancer cells. *Turk J Biochem.* 35: 293-299, 2010

4. Ulukaya E, Acilan C, Yilmaz Y. Apoptosis: Why and how does it occur in biology? *Cell Biochem Func* 29: 468-480, 2011

5. Ulukaya E. Acilan C, Ari F, İkitimur E, Yilmaz Y. A glance at the methods for detection of apoptosis qualitatively and quantitatively. *Turk J Biochem* 36:261-269, 2011

Opening / Keynote Lecture

Genome screening & re-engineering to characterize human genes

Mazhar Adlı

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Recent advances in functional genomics and human cellular models have substantially enhanced our understanding of the structure and regulation of the human genome. However, our grasp of the molecular functions of human genes remains incomplete and biased towards specific gene classes. In this talk, I present a historical perspective on why our understanding of human genes is limited to only ~5% of all protein-coding genes and how we can develop strategies to characterize more genes. Specifically, I present two technologies as powerful tools that enable functional genomics.
Firstly, I will present CRISPR technology, with a specific focus on unbiased genome-level CRISPR screening, as an efficient tool for identifying regulators of critical biological phenotypes. Secondly, I will present various inducible degron technologies with their strengths and weaknesses and our own efforts to use directed evolution to develop a significantly improved novel auxin-inducible degron technology.

Plenary Lecture – 01

The Importance of Tumor Typing for Cancer Patients and Future Perspectives of Molecular Biology of Cancer

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Tumor typing, or cancer subtyping, is a critical process in modern oncology that involves classifying tumors based on their molecular and genetic characteristics. This classification system offers a more precise understanding of a tumor's biology, allowing for tailored treatment strategies and improved patient outcomes.

Why Tumor Typing Matters? Personalized Medicine: Tumor typing enables the development of personalized treatment plans. By identifying the specific molecular alterations driving a patient's cancer, clinicians can select targeted therapies that are more likely to be effective and less likely to cause side effects. Predicting Treatment Response: Certain molecular markers can predict how a tumor will respond to specific treatments. This information helps clinicians choose the most appropriate therapy from the outset, saving time and potentially improving outcomes. Identifying Prognostic Factors: Tumor typing can help identify prognostic factors, such as specific genetic mutations or protein expression levels, that correlate with a patient's disease progression and survival. This information can be used to assess a patient's risk and guide treatment decisions. Early Detection and Prevention: By understanding the molecular mechanisms underlying tumor development, researchers can develop early detection tools and preventive strategies. This could lead to earlier diagnosis and more effective interventions.

Future Perspectives of Molecular Biology of Cancer: The future of cancer research and treatment is closely tied to advances in molecular biology. The focus areas are such as liquid biopsy, which involves analyzing circulating tumor DNA (ctDNA) in blood, is emerging as a powerful tool for early cancer detection, monitoring disease progression, and assessing treatment response. Immunotherapy has revolutionized cancer treatment by harnessing the body's immune system to fight cancer cells. Continued research is focused on developing more effective immunotherapies and identifying biomarkers to predict patient response. Targeted therapies are designed to specifically target the molecular alterations driving cancer growth. As our understanding of cancer genetics deepens, we can expect to see the development of more targeted and effective therapies. Combining different therapies, such as chemotherapy, radiation therapy, immunotherapy, and targeted therapy, can often lead to better outcomes than single-agent therapies. Research is ongoing to optimize these combinations. The ultimate goal of cancer research is to achieve precision medicine, where treatments are tailored to each individual patient based on their unique genetic and molecular profile.

In conclusion, tumor typing is a crucial tool for improving cancer diagnosis, treatment, and patient outcomes. As our understanding of cancer biology continues to evolve, we can expect to see further advancements in molecular diagnostics and targeted therapies.

Plenary Lecture – 02

Mouse models and Critical Considerations in Anticancer drug development

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Mouse models are indispensable in anticancer drug development, offering critical insights into drug efficacy, toxicity, pharmacokinetics, and mechanisms of action. Nevertheless, despite their widespread application, these models face substantial translation challenges, with fewer than 5% of agents demonstrating preclinical efficacy ultimately succeeding in human clinical trials. This high attrition rate highlights the urgent need for strategic model selection, rigorous experimental design, and thorough validation to enhance predictive accuracy. Widely used models, including cell-line-derived xenografts (CDX), patient-derived xenografts (PDX), genetically engineered mouse models (GEMMs), and syngeneic models, each present distinct strengths and limitations in replicating human tumor biology, immune interactions, and therapeutic responses. This lecture will address critical considerations for optimizing mouse-based anticancer drug development, including among others administration vehicle selection, safety and toxicity evaluations, model selection criteria, genetic background effects, standards for ethical conduct and reproducibility. By systematically addressing these factors, the translational relevance of preclinical findings can be improved and more successful, ultimately accelerating the development of effective anticancer therapies.

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Plenary Lecture – 03

Single-cell proteomics to understand cellular heterogeneity and drug response in cancer

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Understanding cancer at the single-cell level is essential for unraveling tumor heterogeneity and identifying the distinct cell populations that contribute to cancer progression and drug resistance. Single-cell analysis reveals cell-specific molecular features, including those of rare or transient cell types, and deepens our knowledge of how tumor microenvironment shape tumor behavior, metastasis, and therapeutic response1,2.

Although advances in single-cell sequencing have accelerated the field forward, mRNA levels often fail to accurately reflect protein abundance. Therefore, single-cell proteomics (SCP) has emerged as a powerful approach, offering direct insights into protein expression which are the key molecules responsible for carrying out cellular processes3. Leveraging cutting-edge LC-MS/MS platforms, SCP now enables the quantification of thousands of proteins from single mammalian cells, each containing 100–200 picograms of protein, which provide insights that remain hidden in traditional bulk proteomic analyses4.

One critical application of SCP lies in understanding drug resistance mechanisms. KRAS G12C, a common mutation in solid tumors, was long considered "undruggable" until the development of covalent inhibitors in 2016. These compounds, including AMG510 (Sotorasib), target the mutant cysteine residue with promising initial results in clinical trials. However, resistance often develops with prolonged treatment, and the molecular basis for this adaptation remains largely unknown5-6. We are currently conducting experiments at the single-cell level to understand distinct proteomic signatures that are associated with survival and resistance.

References

1. Peng, A., Mao, X., Zhong, J., Fan, S., & Hu, Y. (2020). Single-Cell Multi-Omics and Its Prospective Application in Cancer Biology. Proteomics, 20(13), e1900271. https://doi.org/10.1002/pmic.201900271

2. Gohil, S. H., Iorgulescu, J. B., Braun, D. A., Keskin, D. B., & Livak, K. J. (2021). Applying high-dimensional single-cell technologies to the analysis of cancer immunotherapy. Nature reviews. Clinical oncology, 18(4), 244–256. https://doi.org/10.1038/s41571-020-00449-x

3. Vogel, C., & Marcotte, E. M. (2012). Insights into the regulation of protein abundance from proteomic and transcriptomic analyses. Nature reviews. Genetics, 13(4), 227–232. https://doi.org/10.1038/nrg3185

4. Wiśniewski, J. R., Hein, M. Y., Cox, J., & Mann, M. (2014). A "proteomic ruler" for protein copy number and concentration estimation without spike-in standards. Molecular & cellular proteomics : MCP, 13(12), 3497–3506. https://doi.org/10.1074/mcp.M113.037309

5. Li, H. Y., Qi, W. L., Wang, Y. X., & Meng, L. H. (2021). Covalent inhibitor targets KRasG12C: A new paradigm for drugging the undruggable and challenges ahead. Genes & diseases, 10(2), 403–414. https://doi.org/10.1016/j.gendis.2021.08.011

6. Santana-Codina, N., Chandhoke, A. S., Yu, Q., Małachowska, B., Kuljanin, M., Gikandi, A., Stańczak, M., Gableske, S., Jedrychowski, M. P., Scott, D. A., Aguirre, A. J., Fendler, W., Gray, N. S., & Mancias, J. D. (2020). Defining and Targeting Adaptations to Oncogenic KRASG12C Inhibition Using Quantitative Temporal Proteomics. Cell reports, 30(13), 4584–4599.e4. https://doi.org/10.1016/j.celrep.2020.03.021

Closing Lecture

Long non-coding RNAs in cell death and survival

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Long non-coding RNAs (lncRNAs), RNA transcripts longer than 200 nt in length, are novel regulators of both transcriptional and post-transcriptional gene expression involved in numerous cellular processes such as growth, cell death, and differentiation. lncRNAs exist in various biotypes, such as antisense, intergenic, and intronic. RNA sequencing-based approaches are widely used to uncover differentially expressed lncRNAs under the phenotype of interest. We used high and low concentrations of chemotherapeutic drugs, Cisplatin and Doxorubicin, to identify lncRNAs that modulate cellular response under apoptotic and early stress response conditions in HeLa cells. Cells respond quite differently under these conditions by expressing a different set of lncRNAs. Several antisense candidate lncRNAs, such as Death Receptor 5 Antisense 1 (DR5-AS1) and General Transcriptional Factor 2A1 Antisense 1 (GTF2A1-AS1), were then further studied to gain insight into their mode of action. We also used the In Situ Mapping of RNA-Genome Interactome (iMARGI) approach to examine lncRNA-chromatin interactions in the nucleus, which showed a distinct interaction pattern under control and apoptotic conditions in HeLa cells. Lastly, we developed a novel bioinformatic pipeline, sisFindR, to uncover novel intronic lncRNAs in various cancer cell lines. All of these lncRNAs hold promise for biomarkers and RNA therapeutics in different types of cancer.

Invited Speaker – 01

Enhancing CAR-T Cell Therapy: The Impact of Phytohemagglutinin (PHA) Activation on Anti-Tumor Efficacy and T Cell Memory Profile

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Chimeric antigen receptor T (CAR-T) cells represent a promising personalized immunotherapeutic approach, particularly in hematological cancers. This study investigates the effects of Phytohemagglutinin (PHA) activation on CAR-T cell proliferation capacity, memory phenotype, and in vivo stability. CD19-targeted CAR-T cells, generated with two different constructs (incorporating either CD28 or 4-1BB), were activated with either anti-CD3/CD28 or PHA, and evaluated in both in vitro and in vivo acute lymphoblastic leukemia (ALL) models.

CAR19BB-T cells activated with PHA demonstrated higher central memory (Tcm) and stem cell-like memory (Tscm) T cell ratios, reduced exhausted T cell phenotypes, and maintained long-term cytotoxicity. In vivo analyses revealed that PHA-activated CAR-T cells exhibited prolonged persistence, suppressed tumor progression, and preserved organ integrity histologically.

These findings suggest that PHA can serve as an alternative co-stimulatory agent in CAR-T cell manufacturing, enhancing treatment efficacy and cellular stability. Ultimately, this approach offers potential for developing more durable and effective CAR-T cell therapy strategies for clinical application.

Invited Speaker – 02

Next-Generation Chimeric Antigen Receptor T Cell Therapies: Future Perspectives in Clinical Implementation

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Chimeric antigen receptor T cell (CAR-T) therapies have transformed oncology by achieving high remission rates in relapsed or refractory hematologic malignancies. With ongoing expansion into solid tumors and autoimmune diseases, there is an increasing need for a strategic outlook on infrastructure, regulatory alignment, and cost-efficiency. This study aims to evaluate the clinical, regulatory, and production-oriented parameters shaping next-generation CAR-T strategies. Guidelines from the FDA, EMA, etc. were reviewed alongside data from multicenter trials and national registries. Parameters analyzed included antigen diversity, infusion protocols, adverse event profiles, and local manufacturing models, evaluated considering GMP and ATMP compliance.

CD19- and BCMA-directed CAR-T therapies have demonstrated high success rates in acute lymphoblastic leukemia and multiple myeloma. Common adverse events such as cytokine release syndrome and neurotoxicity are clinically manageable. Globally, CAR-T production is shifting from manual to semi-automated systems to lower costs while retaining regulatory quality standards. In Türkiye, ongoing CAR-T initiatives and pilot-scale manufacturing platforms have entered early clinical phases, with national regulatory integration underway. CAR-T therapies are rapidly evolving into scalable and personalized solutions not only for hematologic malignancies but also for solid tumors and autoimmune conditions. Regulatory alignment, autonomous production capacity, and standardized clinical protocols are key for future implementation. Locally produced, cost-effective, and regulation-compliant CAR-T models offer a sustainable pathway for broader clinical integration and equitable patient access.

Key words: CAR-T cell therapy, immunotherapy, ATMP, personalized medicine, cell manufacturing

Invited Speaker – 03

Nerve-Cancer Crosstalk: A Hidden Dimension Driving Pancreatic Cancer Aggressiveness

Didem Karakas Zeybek

Acibadem Mehmet Ali Aydinlar University, Graduate School of Health, Medical Biotechnology Program

Pancreatic ductal adenocarcinoma (PDAC) remains one of the deadliest malignancies worldwide, with a 5-year survival rate barely reaching 12%. Its hallmark features include dense stromal desmoplasia and profound neural invasion, both of which contribute to its aggressive nature. Increasing evidence shows that nerves are not merely passive bystanders in the tumor microenvironment but active participants in tumor progression. Pancreatic tumors stimulate nerve growth and density, while in turn, nerve fibers release signaling molecules that enhance cancer cell proliferation, invasion, metastasis, and therapy resistance.

This bidirectional crosstalk involves complex molecular pathways, including neurotrophic factors, axon guidance molecules, and inflammatory mediators, which together reshape both the nerve and cancer compartments. Clinically, high levels of neural invasion are associated with earlier recurrence, severe neuropathic pain, and poor prognosis. Despite its clinical significance, nerve-cancer interaction remains an underexplored therapeutic target in PDAC.

In our studies, we focus on elucidating the key mechanisms driving nerve-cancer communication, developing experimental models to deepen understanding of neural invasion, and identifying novel therapeutic strategies aimed at disrupting this interplay. We believe that targeting the nerve-tumor axis holds promise not only for halting tumor progression but also for alleviating decreasing pain and improving the quality of life for PDAC patients.

Invited Speaker – 04

Evaluation of the potential role(s) of small molecules in overcoming temozolomide resistance in glioblastoma multiforme: wet lab and in-silico studies

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Glioblastoma multiforme (GBM) accounts for 60 to 70 percent of all gliomas and is categorized as stage IV by the World Health Organization. GBM is the most malignant and aggressive form of glioma, with a poor survival rate of three to six months after diagnosis. Depending on IDH mutation status, primary GBM accounts for 95% of cases associated with IDH_wt, while secondary GBM accounts for 5% of cases associated with IDH_mutation. The only treatment approach is resection of the tumor tissue, followed by radiotherapy and chemotherapy. Temozolomide, an imidazotetrazine prodrug, is the only chemotherapeutic option. Temozolomide is an alkylating agent that removes alkyl groups from the O6 position of guanine in DNA. This activates the DNA repair mechanism, promoting cell death. However, higher MGMT expression repairs DNA mismatches and prevents cell death. There is a strong correlation between MGMT methylation status and TMZ response in GBM. To overcome this resistance mechanism, combination therapy is a strategy to improve the efficiency of TMZ treatment. Our study integrates computational and wet-lab strategies to overcome TMZ resistance, utilizing the principle of combination therapy. We selected cordycepin, a small active metabolite of *Cordyceps militaris (L.)*, as a secondary molecule to apply with TMZ to overcome TMZ resistance. As part of the computational studies, we performed transcriptome analysis with a GBM patient cohort from TCGA to compare TMZ-resistant and TMZ-sensitive cases and select primary targets for testing the Cordy-TMZ response. The possible binding targets of Cordy have been selected via databases. They have also been refined by molecular dynamics and docking studies. To verify the impacts of selected gene candidates on TMZ responses, we conducted experimental studies in 2D in vitro together with Cordy.

Key words: Gliblastoma Multiforme; Temozolomide; Chemo-resistance; Combination therapy

Invited Speaker – 05

Personalized Medicine Approach using Lateral Flow-Based Diagnostic Kit in Ovarian Cancer Screening

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Ovarian cancer (OC) is the third most diagnosed cancer type worldwide and the leading cause of gynecologic cancer deaths. Due to the inadequacy of current treatments, the 5-year survival rate is below 50%. The 5-year survival rate of patients treated in stage I can reach up to 90%, while in stage II, to 70%. In OC diagnosis, several methods are used such as PET/CT, ultrasonography, and MRI, detection of OC-specific biomarkers in the blood. A method capable of detecting tumor sizes that these techniques cannot identify is still lacking in clinical practice. We aimed to evaluate personal clinical results and create new perspectives with "risk score test (RST)" results by screening each patient for OC biomarkers. One of the important research areas is to develop an RST via lateral card testing for OC using biological samples obtained from non-invasive liquid biopsy. RST application is a screening test for potential cancer development. It is a diagnostic, rapid, and easy-to-apply test, and it is possible to determine a personalized risk score by evaluating clinical data results together with protein analysis results using artificial intelligence algorithms. “Lateral flow assay” kits are developed with a qualitative technology and are based on the principle of binding proteins above a certain level with antibodies and observing them linearly on the membrane. The most important advantages of personalized medicine in oncology are the development of patient-specific diagnostic and treatment methods and thus increasing survival rates. As surrogates of cancer, proteins are promising for precise and personalized cancer diagnosis and real-time monitoring cancer progression. Using a panel of identified protein markers as a “cancer signature” may provide improved detection in screening OC for early diagnosis.

Key words: ovarian cancer, lateral flow assays, risk score test, diagnosis

Invited Speaker – 06

Regulation of Ferroptosis by PFKFB Enzymes in Pancreatic Cancer

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Tumor cells reprogram their metabolism to facilitate growth and survival. While rewired metabolism supports malignant features, it is also associated with unique vulnerabilities that may be exploited therapeutically. The family of 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase (PFKFB) enzymes, which are encoded by four separate genes (PFKFB1−4), has emerged as a key activator of aerobic glycolysis, as these enzymes are the only known producers of fructose-2,6-bisphosphate (F2,6BP)—an allosteric stimulator of the glycolytic "gatekeeper" phosphofructokinase-1 (PFK-1) enzyme. Co-expression of PFKFB isozymes is frequently observed in tumor cells, suggesting that PFKFB proteins play non-redundant roles in rewiring metabolism to coordinate with other functions in tumor cells.

In this talk, I will present data, both published and unpublished, that suggest a role for PFKFB2 in the growth, metabolism, and regulation of ferroptosis in pancreatic adenocarcinoma cells. Transient PFKFB2 suppression reduces F2,6BP levels and glycolytic activity in pancreatic adenocarcinoma cells, suggesting a requirement of PFKFB2 activity for setting steady-state F2,6BP levels, despite the co-expression of the PFKFB3 isozyme in these cells. Tumor cells may develop additional metabolic adaptations upon permanent and complete inactivation of genes, leading to unique metabolic vulnerabilities that may be exploited therapeutically. We utilized CRISPR/Cas9-mediated gene targeting to study the long-term consequences of PFKFB2 ablation. PFKFB2-null pancreatic cancer cells exhibit an altered metabolic and growth phenotype. PFKFB2 deletion is associated with the augmentation of the mesenchymal traits of pancreatic cancer cells in vitro, and PFKFB2 expression negatively correlates with the epithelial-mesenchymal transition gene signature in pancreatic cancer patients. Metabolism-focused drug screening reveals the increased sensitivity of PFKFB2-null cells to ferroptosis inducers. Ferroptosis is an iron-dependent cell death that is induced by high reactive oxygen species (ROS) levels, leading to unquenched lipid peroxidation on cellular membranes. The preliminary findings from our ongoing studies suggest that PFKFB2 regulates ferroptosis and warrant further studies investigating PFKFB2 as a potential therapeutic target that may be combined with ferroptosis inducers in pancreatic cancer.

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Invited Speaker – 07

İleri Evre Akciğer Kanserinde Pratiği Değiştiren Gelişmeler ve Kişisel Onkoloji

Orçun Can

Acıbadem Maslak Hastanesi, Tıbbi Onkoloji

İleri evre akciğer kanseri, modern onkolojide hem tanı hem tedavi açısından çok boyutlu yaklaşımlar gerektiren karmaşık bir klinik tablo sunmaktadır. Küçük hücreli dışı akciğer kanseri (KHDAK) ve küçük hücreli akciğer kanseri (KHAK), biyolojik farklılıkları nedeniyle ayrı değerlendirilmekte ve tedavi stratejileri de bu farklılıklar doğrultusunda şekillenmektedir.

KHDAK'de Hedefe Yönelik Tedavilerin Evrimi: KHDAK hastalarının yaklaşık %50'sinde tespit edilebilen sürücü mutasyonlar, tirozin kinaz inhibitörlerinin kullanımını mümkün kılmıştır. EGFR, ALK, ROS1, BRAF V600E, MET ekson 14 skipping, RET, NTRK1/2/3 füzyonları, KRAS G12C, HER2 mutasyonları ve amplifikasyonları bu hedefler arasında yer almaktadır. EGFR mutasyonları (özellikle Exon 19 delesyonu ve L858R), osimertinib gibi üçüncü nesil TKI'lara duyarlılık gösterir. Osimertinib, hem sistemik hem de merkezi sinir sistemi metastazlarında etkili olup, ortalama progresyonsuz sağkalımı 18.9 ay olarak bildirilmiştir (Soria et al., 2018). ALK füzyonu taşıyan hastalarda alectinib, brigatinib, lorlatinib gibi ajanlar MSS metastaz kontrolünde üstünlük sunmaktadır. ROS1 füzyonlarında crizotinib ve entrectinib; BRAF V600E mutasyonlarında dabrafenib + trametinib; MET ekson 14 skipping mutasyonlarında capmatinib ve tepotinib; RET füzyonlarında selpercatinib ve pralsetinib; NTRK füzyonlarında larotrectinib ve entrectinib; HER2 mutasyonlarında trastuzumab deruxtecan; KRAS G12C mutasyonlarında ise sotorasib ve adagrasib etkili hedefe yönelik ajanlardır.

İmmünoterapi: PD-1/PD-L1 Ekseni: İmmün kontrol noktası inhibitörleri, KHDAK'de PD-L1 ekspresyon düzeyine göre seçilmekte olup; yüksek ekspresyonlu (PD-L1 ≥ %50) hastalarda pembrolizumab monoterapisi, düşük veya negatif ekspresyonlarda ise kemoterapi kombinasyonları tercih edilmektedir. KEYNOTE-189 ve IMpower150 çalışmaları, kemoterapi + immünoterapi kombinasyonlarının sağkalım avantajlarını net biçimde ortaya koymuştur (Gandhi et al., 2018; Socinski et al., 2018).

Direnç Mekanizmaları ve Likit Biyopsi: EGFR mutasyonuna yönelik TKI tedavisinde gelişen T790M ve C797S mutasyonları; ALK pozitif tümörlerde G1202R gibi rezistan klonlar, direnç gelişiminin başlıca nedenlerindendir. Bu mutasyonların saptanması için likit biyopsi kullanımı giderek artmakta; plazmada dolaşan tümör DNA'sı (ctDNA), heterojen tümör yükünü yansıtarak tedavi değişiminde yol gösterici olmaktadır (Remon et al., 2020).

KHAK'de Yeni Yaklaşımlar: Küçük hücreli akciğer kanseri, hızlı büyüme hızı ve erken metastatik yayılım eğilimi nedeniyle daha agresif bir klinik seyir gösterir. IMpower133 ve CASPIAN çalışmaları, kemoterapiye atezolizumab veya durvalumab eklenmesinin sağkalımı uzattığını göstermiştir (Horn et

al., 2018; Paz-Ares et al., 2019). Bu gelişmelerle birlikte immünoterapi, KHAK tedavi algoritmalarında kalıcı bir yer edinmiştir.

Gelecek Perspektifi: Yeni nesil immünolojik ajanlar (TIGIT, LAG-3, TIM-3 inhibitörleri), bispesifik antikorlar (ör. amivantamab), antikor-ilaç konjugatları (ör. trastuzumab deruxtecan, datopotamab deruxtecan), mRNA aşıları ve CAR-T hücre terapileri; hem KHDAK hem de KHAK'de kişiselleştirilmiş tedavi olanaklarını genişletmektedir. Aynı zamanda mikrobiyotanın immünoterapiye yanıt üzerindeki etkisini inceleyen çalışmalar, diyet modifikasyonları ve probiyotik takviyeleri gibi yeni terapötik pencereler sunmaktadır (Routy et al., 2018).

Sonuç: Akciğer kanseri yönetiminde, moleküler profillemenin yön verdiği hedefe yönelik ajanlar, immünoterapiler ve direnç yönetimi gibi başlıklarda kaydedilen ilerlemeler, klinik pratiği köklü biçimde dönüştürmüştür. Bu gelişmeler ışığında, kişiselleştirilmiş tedavi paradigması artık istisna değil, standarttır.

Kaynakça

Gandhi, L. et al. (2018). Pembrolizumab plus chemotherapy in metastatic non–small-cell lung cancer. New England Journal of Medicine, 378(22), 2078–2092. https://doi.org/10.1056/NEJMoa1801005

Horn, L. et al. (2018). First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. New England Journal of Medicine, 379(23), 2220–2229. https://doi.org/10.1056/NEJMoa1809064

Paz-Ares, L. et al. (2019). Durvalumab with platinum–etoposide in small-cell lung cancer. New England Journal of Medicine, 381(1), 20–31. https://doi.org/10.1056/NEJMoa1916345

Peters, S. et al. (2017). Alectinib versus crizotinib in untreated ALK-positive non–small-cell lung cancer. New England Journal of Medicine, 377(9), 829–838. https://doi.org/10.1056/NEJMoa1704795

Remon, J. et al. (2020). Liquid biopsy in oncology: A consensus paper of the Spanish Society of Medical Oncology (SEOM). Clinical & Translational Oncology, 22(7), 827–834. https://doi.org/10.1007/s12094-020-02293-3

Routy, B. et al. (2018). Gut microbiome influences efficacy of PD-1–based immunotherapy against epithelial tumors. Science, 359(6371), 91–97. https://doi.org/10.1126/science.aan3706

Socinski, M. A. et al. (2018). Atezolizumab for first-line treatment of metastatic nonsquamous NSCLC. New England Journal of Medicine, 378(24), 2288–2301. https://doi.org/10.1056/NEJMoa1716948

Soria, J. C. et al. (2018). Osimertinib in untreated EGFR-mutated advanced non–small-cell lung cancer. New England Journal of Medicine, 378(2), 113–125. https://doi.org/10.1056/NEJMoa1713137

Invited Speaker – 08

Cancer and Ion Channels

Damien Bell

Sophion Bioscience

Invited Speaker – 09

Elektrik alan terapisi: Kanser tedavisinde yeni bir modalite

Murat Köylü

Ege Üniversitesi Tıp Fakültesi Radyasyon Onkolojisi Anabilim Dalı

Invited Speaker – 10

3D Organoid Kültürler ve Kanserlerde Kullanım Alanları

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3D Organoid çalışmaları, in vivo ortamları mimikleyen yapılarından dolayı gelişimsel ve hastalık biyolojisi araştırmalarında, kök hücre biyolojisi, kanser biyolojisi, ilaç güvenlik ve etkinlik testleri, organ replasman tedavisi ve kişiselleştirilmiş tedavilerde devrim yaratmıştır. 2D kültürlerin, hücre-hücre ve hücre-matriks etkileşimlerinde, tümör sinyalizasyonunda ve ilaç yanıtında önemli olan doğal mikro ortamdan yoksun olması ilaç/moleküllerin klinik denemelerinde etkinliklerinin daha zayıf bulunmasıyla terapötiklerin keşfini geciktirmektedir. Hem sağlıklı hem de hasta dokulardan oluşturulan organoidlerle laboratuvarda hasta hücrelerinin çoğaltılması önemlidir. Organoid kültürleri genetik stabiliteyi korurken uzun vadede de sürdürülebilirler. Organoidler, kalıtsal hastalıklar, bulaşıcı hastalıklar, metabolik bozukluklar ve kanserde hücrenin kaderini açıklamanın yanı sıra embriyonik gelişim, moleküler mekanizmalar, rejeneratif hücre tedavileri, organ nakli ve konak-mikrop etkileşimleri gibi süreçlerin incelenmesinde kullanılan sistemlerdir. 3D kültürde oluşturulan organoidler, orijinal organla aynı hücre heterojenliğine ve yapıya sahiptir. Bağırsak, kolon, mide, pankreas, prostat, karaciğer, beyin vb. gibi farklı dokulardan elde edilen kök hücrelerden organoidler üretilebilmiştir. Her organoid hattı, genetik ve transkripsiyonel bilgileri ilaç duyarlılığına bağlayan bir veri tabanı oluşturmak için genom dizilimi, ifade profili ve bilinen ilaçlarla ilaç testi kullanılarak karakterize edilir. Kanser araştırmalarında kullanılan kanser 3D organoid sistemleri bulunmaktadır.

Organoidlerin kanser tedavisindeki uygulamaları: hassas tıp, gen düzenleme, klinik araştırma, hastalık modelleme, temel araştırma ve yeni ilaç keşfi alanlarındadır. Hasta tümör doku organoidleri, in vivo tümörlere histolojik ve işlevsel benzerlik gösterir ve bu organoid modelleri, kanserin tedavisinde kullanılan ilaçlara karşı gelişen direnci tahmin etmek ve kişiselleştirilmiş tıpta genomik analizle birleştirilmiş yüksek verimli ilaç taraması için en etkili kanser tedavisini belirlemek ve kişiselleştirilmiş tıbbı ilerletmek için güçlü araştırma araçları haline gelmektedir.

Organoid teknolojisinin yapay zeka ve mikroakışkanlarla entegrasyonu, büyük ölçekli, hızlı ve uygun maliyetli ilaç toksisitesi ve etkinlik değerlendirmelerini artırarak hassas tıpta ilerlemeyi hızlandırmıştır. Yüksek performanslı malzemelerin, 3D baskı teknolojisinin ve CRISPR Cas9 sistemleri ile gen düzenlemenin çalışmalara dahil edilmesi organoid çalışmalarını bir çok alanda öne çıkarmaktadır.

Invited Speaker – 11

GBM'e Meydan Okumak: Zihnin Sinirlarinda Yenilikçi Tedavi Stratejilerinin Peşinde

Gamze Tanrıöver

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Introduction and Aim: Glioblastoma Multiform (GBM) is the most prevalent brain tumor in adults with an annual incidence of 3.19 per 100,000 population. Upon diagnosis, patients undergo surgical resection followed by Temozolomide (TMZ) administration and radiotherapy. However, investigating new therapeutic agents is crucial. TAS-115 is a multi-receptor tyrosine kinase inhibitor that c-Met, VEGFR, and PDGFR. Our study was designed the hypothesis that "TAS-115 limits proliferation and invasion by inhibiting c-MET/HGF-mediated pathways in GBM". The aim of study was to evaluate the effects of TAS-115 on GBM.

Materials and Methods: In this study, TMZ-sensitive (U87MG) and TMZ-resistant (T98G, GL261) GBM cells were used. Groups included Control, Vehicle, TMZ, TAS-115, and TMZ+TAS-115. IC_{50} values of TMZ and TAS-115 were determined and also, cell proliferation were evaluated via clonogenic assay. The motility potentials of cells were assessed by migration and invasion assays. c-MET/HGF expression was analyzed via immunocytochemistry. TAS-115 was conjugated with nanoparticles and administered to GL261 cells. Its BBB permeability was evaluated by *in silico* and confirmed *in vitro* using the PAMPA assay.

Results: The administration of TMZ and TAS-115 demonstrated reduction in GBM cell proliferation. Colony-forming and migratory capacities of tumor cells were decreased. Protein levels of p-ERK, p-MET, p-mTOR, p-STAT3, and NF-κB were reduced compared to the control group. The angiogenesis marker p-VEGFR2 was decreased. In GL261 cells, the IC_{50} value of TAS-115+UCNP was determined. Computational analyses revealed that only four TAS-115 metabolites failed to cross the BBB. PAMPA assay showed that TAS-115 crosses the BBB less efficiently than TMZ.

Discussion: Our study, it was demonstrated that both TMZ and TAS-115 reduce motility and proliferation in GBM cells. Although the effects of TMZ on GBM are well-documented in the literature, TAS-115 hasn't evaluated in this tumor type. Therefore, we believe that our findings address this gap in the literatüre.

Key words: Glioblastoma Multiforme, Temozolomide, TAS-115, c-MET/HGF

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Invited Speaker – 12

The Critical Role of Structural Biology Studies in Targeted Drug Development

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Determining the correct biological target is one of the most critical decisions in the drug development process, both from a scientific and strategic perspective. The accuracy of target selection directly influences the efficacy, safety, and personalization of the resulting treatment. Structural biology plays a key role in this context by analyzing the three-dimensional architecture of intracellular biomolecules at the atomic level, allowing for a detailed understanding of their functions. Since molecular structure dictates function, structural abnormalities are frequently implicated in disease pathogenesis. Thus, insight into protein structures enables the development of effective and selective therapeutic strategies.
Three principal techniques widely used in structural biology are X-ray crystallography, cryo-electron microscopy (Cryo-EM), and nuclear magnetic resonance (NMR) spectroscopy. X-ray crystallography involves directing high-energy X-rays at purified and crystallized protein samples. These rays produce diffraction patterns by interacting with atoms in the crystal, which are then translated into three-dimensional atomic models using computational algorithms. This method is particularly powerful for identifying active sites, ligand-binding pockets, and functional domains of proteins with high resolution.
Cryo-EM offers a different advantage by allowing the observation of macromolecular structures in their near-native state. Proteins or protein complexes are rapidly frozen at cryogenic temperatures and imaged under an electron microscope from various angles. The collected two-dimensional images are computationally reconstructed into three-dimensional structures. Cryo-EM is especially useful for large, flexible, or non-crystallizable complexes, requiring only small sample volumes while preserving the biomolecule's physiological integrity.
NMR spectroscopy is employed primarily for small to medium-sized proteins in solution. It measures magnetic resonance signals from atomic nuclei using radiofrequency pulses. These signals provide information about interatomic distances, molecular conformations, and dynamic interactions. NMR is particularly valuable for studying protein flexibility and time-dependent structural changes. Isotope labeling techniques enhance resolution, enabling more complex structural determinations.
Collectively, these three techniques allow for precise mapping of functionally relevant regions, disease-causing mutations, and drug-binding interfaces in proteins. This structural knowledge provides a robust foundation for rational drug design and targeted therapy. Experimental findings are further supported through biological activity assays, molecular techniques, and various animal models, ensuring the relevance and applicability of the structural insights.
In addition, artificial intelligence tools such as AlphaFold have transformed protein structure prediction. AlphaFold predicts protein structures directly from amino acid sequences with remarkable accuracy.

While it significantly speeds up structure determination, it has limitations, including poor performance with complex assemblies, intrinsically disordered regions, or ligand-bound forms. Therefore, AI-based predictions complement but do not replace experimental methods.

In conclusion, structural biology—through both traditional methods and AI-driven innovations—provides the essential atomic-level insight needed to develop precise, efficient, and personalized therapies, forming the cornerstone of modern drug discovery.

Keywords: Structural biology, targeted therapy, X-ray crystallography, Cryo-EM, nuclear magnetic resonance (NMR) spectroscopy

Invited Speaker – 13

Synthesis and Cytotoxicity Evaluation of Novel Endoperoxide Derivatives as Potential Anti-Cancer Agents

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Introduction and Aim: Nowadays, design and synthesis of novel organic molecules or isolation of natural products from plants have been gained big importance for the treatment of cancer and other diseases. Endoperoxides are a group of drugs that possess the most rapid action of all current drugs against malaria. Last decades, there have been many research including biological properties of artemisinin as endoproxide. However, there are a few studies for the design and synthesis of novel artemisinin derivatives. Therefore, scientists have been tried to find best hybrid molecules consisting artemisinin and biologically known organic molecules.

Materials and Methods: In this study, artemisinin-benzothiophene, artemisinin-indole, artesunate-benzothiophene, artesunate-indole and artemisinin-thymol hybrid derivatives have been synthesized. Initially, 3-iodobenzothiophene and 3-iodoindole derivatives were obtained with high selectivity and yields by using Sonogashira coupling reactions and electrophilic cyclization reactions. Then, benzothiophene/indole derivatives with aldehyde functional group were synthesized using Suzuki-Miyaura coupling reactions in the presence of palladium catalyst. These isolated aldehyde derivatives converted into i) corresponding alcohol structures by reduction reactions ii) corresponding carboxylic acid derivatives by oxidation reactions. Finally, Steglich esterification reaction was used for the synthesis of designed hybrid molecules.

Results: Novel artesunate-benzothiophene, artesunate-indole and artsunate-benzofuran were synthesized with high yields. When the cytotoxic effects of hybrid structures were analyzed, it was found that they have cytotoxic effects and were effective in Caco-2 (EC50: 7,14 μM).

Discussion: Herein, It were found that these artemisinin based heterocyclic compounds displayed very high activity for cancer cell lines. They will be new drug candidates as anticancer agents.

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Invited Speaker – 14

Anticancer Agents from Natural Products

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Natural products have emerged as a prolific source of novel anticancer agents, offering a diverse array of chemical scaffolds with unique mechanisms of action (Newman and Cragg, 2016). Recent investigations have focused on isolating and characterizing bioactive compounds from various plants, marine organisms, and microorganisms that exhibit potent cytotoxicity against cancer cells (Zhang et al., 2019). In vitro and in vivo studies have demonstrated that these natural compounds can induce apoptosis, inhibit cell proliferation, and interfere with key signaling pathways involved in tumor growth and metastasis (Kingston, 2007). Natural product-derived agents such as taxanes, camptothecines and vinca alkaloids have not only provided a basis for the development of existing chemotherapeutics, but have also inspired the synthesis of new analogs with improved efficacy and reduced toxicity (Schmidt, 2009). Furthermore, advances in high-throughput screening, combinatorial chemistry, and molecular docking have accelerated the identification and optimization of these compounds (Li et al., 2011). Despite promising preclinical results, challenges remain in translating these findings into clinical applications, including issues related to bioavailability, resistance, and the inherent complexity of natural extracts. Future research directions include the integration of omics technologies and advanced drug delivery systems to enhance therapeutic indices and overcome these limitations. Collectively, these findings underscore the importance of natural products in the ongoing search for effective anticancer therapies and provide a framework for the development of next-generation anticancer drugs.

Key words: Natural products, taxane, anticancer

References

1. Newman, D. J. and Cragg, G. M. (2016). *Natural Products as Sources of New Drugs from 1981 to 2014*. Journal of Natural Products.
2. Zhang, A., Sun, H., Wang, X., & Wang, P. (2019). *Recent Advances in Natural Product-Based Cancer Therapeutics*. Trends in Pharmacological Sciences.
3. Kingston, D. G. (2007). *Modern Natural Products Drug Discovery and its Relevance to Biodiversity Conservation*. Journal of Natural Products.
4. Schmidt, E. W. (2009). *Natural Product Discovery: Past, Present, and Future*. Journal of Industrial Microbiology and Biotechnology.
5. Li, J., et al. (2011). *High-Throughput Screening for Anticancer Natural Products*. Bioorganic & Medicinal Chemistry.

Invited Speaker – 15

Novel Approaches to Leukemia Treatments and Drug Repurposing Strategies

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Drug repurposing, the strategy of identifying new therapeutic uses for existing medications, has emerged as a promising approach for leukemia treatment, offering significant time and cost advantages compared to traditional drug development. Leukemia, a heterogeneous group of hematologic malignancies characterized by the abnormal proliferation of leukocytes, continues to present significant treatment challenges, including resistance and relapse after standard therapies. Consequently, drug repurposing has become increasingly attractive to quickly expand therapeutic options.

Recent studies leveraging bioinformatics and high-throughput screening have identified several promising repurposing candidates for leukemia. Common examples include antimicrobial, antiviral, anti-inflammatory, and cardiovascular medications. Furthermore, integrative approaches combining computational biology, genomic analysis, and pharmacological databases have streamlined the identification of novel repurposing targets. Techniques such as virtual screening, transcriptomic analyses, and connectivity mapping facilitate rapid evaluation of drug efficacy, significantly accelerating preclinical validation. Repurposed drugs are particularly advantageous due to their well-characterized pharmacokinetics, known safety profiles, and existing regulatory approvals, allowing expedited translation from laboratory research to clinical application.

We have also identified novel candidates for the treatment of different type of leukemias by using computational approaches and validated by in vitro studies. We have identified various new targets for myeloid leukemias including MPO, CTSG, BEX1 and ELANE genes. The studies on acute lymphoblastic leukemia has shown various new targets as potential therapeutic options including different microRNAs such as hsa-let-7a-5p, hsa-miR-100-5p, hsa-miR-101-3p as novel targets for ALL treatment.

Collectively, these studies illustrate the power of integrative bioinformatics and in vitro validation in accelerating the identification of novel leukemia therapies. By leveraging publicly available datasets and FDA-approved compounds, these approaches offer cost- and time-effective alternatives to traditional drug development, with significant translational potential.

Short Talk – 01

Cure-ious Artificial Intelligence for Small Molecule Design to Target Cancer Hallmarks

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Cancer remains a formidable global health challenge [1,2], mainly due to its complex and multifaceted biological mechanisms, collectively referred to as the "Hallmarks of Cancer" [3,4]. These hallmarks, including sustained proliferative signaling, evasion of growth suppressors, resistance to cell death, induction of angiogenesis, and avoidance of immune destruction, represent critical therapeutic targets in modern oncology. Recent advancements in Artificial Intelligence (AI), Bioinformatics, and Computational-Aided Drug Design have revolutionized the drug discovery process [5], offering unprecedented opportunities for developing small molecule inhibitors with enhanced specificity, efficacy, and safety profiles. This review provides a comprehensive overview of AI-powered methodologies integrated with bioinformatics analyses to accelerate the identification, design, and optimization of small molecules that precisely target cancer hallmarks. By combining machine learning, deep learning, structure- based, and ligand-based approaches, these innovative strategies facilitate the efficient screening of chemical libraries, de novo design of novel molecular scaffolds, and predictive modeling of protein-ligand interactions. Advanced techniques such as molecular docking and molecular dynamics simulations enhance the accuracy of binding affinity predictions, enabling the discovery of high-affinity molecules with therapeutic potential across various cancer processes. Integrating bioinformatics tools aids in target prioritization, mechanistic insights, and the identification of novel therapeutic targets, ensuring that designed molecules align with the complex biology of cancer. Additionally, applying quantitative structure-activity relationship models and generative AI techniques, including Generative Adversarial Networks and Variational Autoencoders, has significantly contributed to the rational design of molecules with optimized pharmacokinetic and pharmacodynamic profiles. These models not only improve hit-to-lead conversion rates but also enhance Absorption, Distribution, Metabolism, Excretion, and Toxicity predictions, minimizing the risk of late-stage drug development failures. Artificial intelligence bridges in silico predictions with clinical applications, paving the way for the development of precise and targeted cancer therapies.

Key words: AI-powered drug discovery, Computational-aided drug design (CADD), Cancer hallmarks, Small molecule inhibitors, Bioinformatics

References:

[1] Ferlay, J., Laversanne, M., Ervik, M., Lam, F., Colombet, M., Mery, L., Piñeros, M., Znaor, A., Soerjomataram, I., & Bray, F. (2024). *Global Cancer Observatory: Cancer Tomorrow (version 1.1).* Lyon, France: International Agency for Research on Cancer. Retrieved February 8, 2024, from https://gco.iarc.who.int/tomorrow/en

[2] World Health Organization. (n.d.). *Cancer*. Retrieved February 8, 2024, from https://www.who.int/news-room/fact-sheets/detail/cancer

[3] Hanahan, D., & Weinberg, R. A. (2000). The hallmarks of cancer. *Cell*, *100*(1), 57–70. https://doi.org/10.1016/S0092-8674(00)81683-9

[4] Hanahan, D., & Weinberg, R. A. (2011). Hallmarks of cancer: The next generation. *Cell*, *144*(5), 646–674.

[5] Cui, W., Aouidate, A., Wang, S., Yu, Q., Li, Y., & Yuan, S. (2020). Discovering anti-cancer drugs via computational methods. *Frontiers in Pharmacology*, *11*, 733.

Short Talk – 02

Post-transcriptional and Post-Translational Regulation of S6K2 May Confer Its Stability and Function, Provoking Resistance to Apoptosis in Cancer

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S6K2, an effector of PI3K/Akt/mTOR signaling pathway, is the newer member of p70 S6 kinase family. S6K2 had once been regarded as a redundant protein due to its high homology with S6K1, but recent studies have revealed that they have different substrates and exert different functions. Even both proteins contribute to breast cancer cell survival via different routes. S6K1 exerts a negative feedback loop via phosphorylating IRS-1. Therefore, therapeutic approaches targeting S6K1 faces important setbacks. On the other hand, S6K2 enforces a positive feedback loop via Akt which strengthens breast cancer cell survival, pointing out a potential spotlight. In addition to this role, S6K2 contributes to breast and lung cancer cell survival via complexing with anti-apoptotic proteins B-Raf and PKCε and derepressing the translation of anti-apoptotic proteins Bcl-XL and XIAP. Regarding these roles, many mechanisms underlying the stability and the functions of S6K2 still remain to be discovered. Lysine acetylation and arginine methylation of S6K2 were reported to stabilize cellular S6K2 level. Also, S6K2 was shown to be ubiquitinated but the responsible ubiquitin ligase is still unknown. Despite potential sites, nothing is currently known about sumoylation of S6K2 as well. Moreover, the mechanism in which S6K2 signaling is terminated, in other words, the phosphatase which dephosphorylates S6K2, is yet to be uncovered. Until recently, three microRNAs were displayed to regulate S6K2 (miR-193a-3p, miR-193a-5p and miR-1273g-3p). On the other hand, the potential binding sites may highlight other S6K2-regulatory microRNAs. In addition, any long non-coding or circular RNAs regulating S6K2 stability or function still needs to be unraveled. The uncovering of all these aforementioned obscurities about the post-transcriptional and post-translational mechanisms regulating S6K2 will enable us to target the protein, sensitizing breast cancer cells to apoptotic stimuli.

References:

1. Pardo OE and Seckl MJ. (2013) S6K2: The Neglected S6 Kinase Family Member. *Front Oncol*, 3(July), 191.

2. Pardo OE, Arcaro A, Salerno G, Tetley TD, Valovka T, Gout I, Seckl MJ. (2001) Novel cross talk between MEK and S6K2 in FGF-2 induced proliferation of SCLC cells. *Oncogene*. 20(52), 7658-67.

3. Pardo OE, Wellbrock C, Khanzada UK et al. (2006) FGF-2 protects small cell lung cancer cells from apoptosis through a complex involving PKCepsilon, B-Raf and S6K2. *EMBO J*. 25(13):3078-88.

4. Sridharan S and Basu A. (2011) S6 kinase 2 promotes breast cancer cell survival via Akt. *Cancer Res*. 71(7), 2590–2599.

5. Sever NI and Cengiz-Sahin S. (2019) S6K2 promises an important therapeutic potential for cancer. *Future Oncol.* 15(1):95-102.

Short Talk – 03

Targeting HGSOC with Purine-Based Nucleobase Analogues: Selective Cytotoxicity via Apoptotic and Autophagic Pathways

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Introduction and Aim: Ovarian cancer (OC) is the fifth leading cause of cancer-related death among women, with high-grade serous ovarian cancer (HGSOC) being its most aggressive and common subtype. Although 85% of HGSOC patients initially respond to surgery and platinum-based chemotherapy, 15–20% show primary resistance, and approximately 25% relapse within six months. Despite the incorporation of PARP inhibitors into treatment regimens, resistance remains a significant clinical challenge.

In search of new therapeutic strategies, purine analogues have drawn attention due to their structural versatility and ability to modulate diverse cellular processes. Although compounds like cladribine and fludarabine are clinically approved for other cancers, their potential in ovarian cancer is not fully understood.

Materials and Methods: This study evaluated the cytotoxicity of 18 newly synthesized purine/pyrimidine nucleobase analogues using the NCI-SRB assay in three HGSOC cell lines (OVCAR-3, OVSAHO, Kuromachi) and a non-malignant epithelial line (HGRC1). Compounds 31 and 32, which showed the highest cytotoxicity, were selected for further analysis. Their effects on cell cycle progression (PI staining), apoptosis (Annexin V and Caspase 3/7 assays), and intracellular signaling (Western blotting) were investigated. The involvement of autophagy was also studied using pharmacological inhibitors and additional assays.

Results: Results revealed a significant increase in the SubG1 population, indicating programmed cell death, accompanied by concurrent activation of apoptotic and autophagic pathways upon treatment with compounds 31 and 32. Notably, these compounds displayed minimal toxicity in non-cancerous cells, indicating a degree of selectivity for malignant cells.

Discussion: In conclusion, purine analogues 31 and 32 exhibit promising anti-tumor activity in HGSOC by simultaneously triggering apoptosis and autophagy. These findings support their potential as dual-mechanism therapeutic agents, warranting further validation through ex vivo, in vivo, and in silico studies.

Key words: HGSOC, purine analogues, apoptosis, autophagy

Short Talk – 04

Likit Biyopsi Temelli Çoklu Kanser Erken Tanı (MCED) Testlerinin Potansiyeli ve Kısıtlılıkları

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Kanserin erken tanısı, tedavi başarısını artıran en önemli faktörlerden biridir. Son yıllarda likit biyopsi yöntemleriyle geliştirilen çoklu kanser erken tanı (MCED) testleri, tek bir kan örneği üzerinden çok sayıda kanser tipini eşzamanlı olarak tespit etme imkânı sunmaktadır. Bu testler, dolaşımdaki tümör DNA'sı (ctDNA), DNA metilasyon profilleri, dolaşımdaki tümör hücreleri (CTC) ve protein bazlı biyobelirteçler kullanarak çok sayıda farklı kanser tipini yüksek özgüllük ile tanımlayabilmektedir.

Galleri, CancerSEEK ve Trucheck gibi öne çıkan MCED testlerinin klinik performansları yapılan çalışmalarda kapsamlı biçimde değerlendirilmiştir. Galleri testi, cfDNA metilasyon analiziyle 50'den fazla kanser tipini tespit edebilirken, erken evre kanserlerde duyarlılığı (%17-40) ileri evrelere göre (%77-90) düşük kalmaktadır. CancerSEEK testi ise protein ve mutasyon temelli belirteçler kullanarak %70 civarında genel duyarlılığa ulaşmakta, ancak erken evrede duyarlılık yine kısıtlı kalmaktadır. Trucheck testi ise dolaşımdaki tümör hücrelerini kanser tipine bağlı olarak yüksek duyarlılık (%65-89) ve özgüllük (%96-99) ile belirleyebilmektedir.

MCED testlerinin potansiyeli yüksek olsa da erken evre kanserlerin tespitinde halen belirgin kısıtlılıklar bulunmaktadır. Yanlış negatif sonuçlar, bireylerin standart tarama yöntemlerinden uzaklaşmasına neden olabilirken, yanlış pozitif sonuçlar da gereksiz ileri tanı prosedürlerine ve psikolojik strese yol açabilmektedir. Ayrıca, MCED testlerinin klinik yararının, sağkalım ve yaşam kalitesi gibi sonuçlarla netleşmesi gerekmekte olup, bu hedef doğrultusunda büyük ölçekli klinik çalışmalar halen devam etmektedir.

Sonuç olarak, likit biyopsi temelli MCED testleri, kanser taramasında devrim niteliğinde yenilikler vaat etmekle birlikte, klinik uygulamadaki kısıtlılıkları ve hasta yönetimindeki etkinlikleri daha fazla kanıtla desteklenmelidir.

Anahtar kelimeler: Çoklu kanser erken tanı (MCED), likit biyopsi, cfDNA, ctDNA, dolaşımdaki tümör hücreleri (CTC).

Referanslar:

Wade, R., Nevitt, S., Liu, Y., Harden, M., Khouja, C., Raine, G., ... & Dias, S. (2025). Multi-cancer early detection tests for general population screening: a systematic literature review. *Health Technology Assessment*, *29*(2), 1.

Datar Cancer Genetics - Europe. (4 Nisan 2025). *Trucheck – Early cancer screening*. https://www.datarpgx.de/en/trucheck-en/

Short Talk – 05

Synergistic Effect of Temozolomide and EGFR Inhibitor on GBM Cell Line in a 3D GelMA Hydrogel Model: A Comparative Analysis with 2D Culture

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Glioblastoma multiforme (GBM) is a malignant brain tumor characterized by high proliferation and resistance to therapy. Temozolomide (TMZ) is widely used as a standard chemotherapeutic agent; however, resistance development remains a major clinical challenge. Epidermal Growth Factor Receptor (EGFR) is frequently overexpressed in GBM, and inhibiting this pathway may help overcome drug resistance. This study investigated the combined effect of TMZ and an EGFR inhibitor in a 3D GelMA hydrogel model compared to a 2D culture system. U87 cells were cultured in 2D and encapsulated in 3D GelMA hydrogels. Control, TMZ, EGFR inhibitor, and combined treatment groups were established. Cell viability (SRB, Live/Dead), apoptosis (Annexin V/PI, Caspase 3/7 activity), wound healing assays, and gene expression (qPCR) analyses were performed. In 2D, both TMZ and Erlotinib significantly reduced viability and induced apoptosis. However, in the 3D model, the efficacy of individual treatments was significantly reduced. This suggests that the 3D environment more accurately reflects tumor-specific resistance mechanisms. Conversely, combination therapy showed the most substantial reduction in viability and most potent apoptosis induction in both models, with a significant apoptotic response even in 3D. Wound healing analysis showed that migration and wound closure were significantly inhibited in the combination group in 3D. Considering all these findings, combination therapy demonstrates substantial potential in overcoming resistance to GBM treatment.

Key Words: Glioblastoma (GBM), Temozolomide (TMZ), EGFR inhibition, 3D GelMA hydrogel model

Short Talk – 06

Kanser ve Diyabet

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Kanser ve diyabet, sağlık açısından tehdit oluşturan iki kronik hastalıktır. Özellikle tip 2 diyabet, meme, pankreas, kolon, karaciğer ve rahim kanseri gibi çeşitli kanser türleriyle ilişkilendirilmiştir. Bu hastalıklar arasındaki ilişki netlik kazanmamış olup, ortak risk faktörleri ve biyolojik mekanizmalar diyabetli bireylerde kanser görülme oranının daha yüksek olmasına katkıda bulunmaktadır.

Diyabette kanser riskini artıran faktörler hiperglisemi ve insülin direnci olabilir. Bu mekanizmalar, hücre çoğalmasını tetikleyerek kanser gelişimini teşvik edebilir. Ayrıca, obezite, sağlıksız beslenme, sigara kullanımı, alkol tüketimi ve yetersiz fiziksel aktivite gibi yaşam tarzı faktörleri de hem diyabetin hem de kanserin ortaya çıkmasında önemli bir rol oynamaktadır.

Epidemiyolojik çalışmalar, diyabetik hastalarda kanserin daha yaygın olduğunu ve bu hastaların da kansere bağlı ölüm oranlarının daha yüksek olduğunu göstermektedir.

Diğer yandan, özellikle metformin gibi bazı diyabet ilaçları, potansiyel olarak kanser önleyici etkilere sahip olabilir. Metformin, insülin seviyelerini artırmadan kan şekeri seviyelerini düzenleyerek hücresel büyümeyi baskılayabilir ve böylece kanser riskini azaltabilir. Bu özelliği sayesinde, metformin olası bir anti-kanser ajanı olarak değerlendirilmektedir.

Sonuç olarak, kanser ve diyabet arasındaki ilişki karışık olmakla birlikte, her iki hastalığın önlenmesi ve tedavi stratejilerinin geliştirilmesi açısından bu konu ile ilgili daha fazla araştırmaya ihtiyaç bulunmaktadır.

Anahtar Kelimeler: Kanser, diyabet, hiperglisemi, insülin direnci

Short Talk – 07

The role of antihistamines in cancer treatment

Didem Seven

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Certain antihistamines, commonly used to alleviate allergy symptoms, are being researched as potential cancer treatments due to their immunomodulatory, anti-angiogenic, and tumor-suppressive properties. Preventing histamine receptors from being activated can lead to an increase in antitumor immunity, a decrease in the immunosuppressive effects of tumors, and the inhibition of angiogenesis. H2 antagonists such as cimetidine have demonstrated potential in extending survival rates for specific types of cancer, whereas medications like loratadine may improve the effectiveness of chemotherapy. Furthermore, antihistamines can alter the tumor microenvironment by decreasing inflammation and fibrosis.

A recent study encompassing various cancer types, such as melanoma, lung, and breast cancer, demonstrated that allergic responses mediated through the histamine-HRH1 signaling axis promote tumor progression and are associated with resistance to immunotherapy in both preclinical and clinical settings. Increased expression of histamine and its receptors (H1R–H4R) has been observed in multiple tumor cell types and within the tumor microenvironment, highlighting their potential contribution to cancer progression. Previously, in a large scale retrospective study in lung cancer patients, the effect of loratadine was shown with improved survival rates

In our laboratory, the effects of desloratadine, one of the most commonly used antihistamines, were investigated in cancer cells. The IC50 value of desloratadine was determined. It was demonstrated that desloratadine impacts the viability of lung, head and neck, and prostate cancer cells and its effects on cell cycle progression, colony formation, sphere formation, and stemness were evaluated. Consistent with findings in the literature, our results showed that the antihistaminic drug inhibited tumor progression in cancer cell lines. Ongoing studies and clinical trials further support their potential as adjunctive therapies, particularly when combined with immunotherapy. These findings highlight the promise of antihistamines as a potential candidate for repurposing in cancer therapy.

Short Talk – 08

ERK5's Dark Side: Unraveling Its Role in Hormone-Driven Cancers

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ERK5 (extracellular signal-regulated kinase 5), also referred to as Big mitogen-activated protein kinase-1 (Bmk1), is the most recently identified member of the mitogen-activated protein kinase (MAPK) family. Encoded by the MAPK7 gene, ERK5 exhibits broad expression across human tissues. Its activation is triggered by diverse stimuli, including growth factors, osmotic stress, and oxidative stress. Upon ligand binding to their respective receptors, ERK5 undergoes phosphorylation at its activation loop motif by the upstream kinase MEK5, leading to its activation. Studies analyzing cancer tissue samples and cell lines have revealed that MEK5 and/or ERK5 are frequently overexpressed in several prevalent human cancers, including breast cancer, prostate cancer, oral squamous cell carcinoma, and hepatocellular carcinoma. This overexpression is often associated with poor clinical outcomes. The involvement of ERK5 in cancer progression stems from its capacity to enhance cell proliferation and survival, thereby accelerating tumorigenesis, as well as its role in promoting cell migration and invasion, which facilitates metastasis. In this presentation, we critically examine the role of ERK5 in hormone-dependent malignancies, integrating existing literature with our experimental findings to elucidate its mechanistic contributions and therapeutic implications.

Key words: ERK5, MAPK7, androgen receptor, endometrial cancer

Short Talk – 09

Investigating circGPRC5A-Mediated Regulation of GPRC5A Gene Expression in Breast Cancer

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Introduction and Aim: Breast cancer is the most common type of cancer and the leading cause of cancer-related deaths worldwide. Its pathology has been associated with the dysregulation of numerous genes and various epigenetic mechanisms. Circular RNAs (circRNAs), covalently closed noncoding RNAs, have emerged as important players in breast cancer pathology. Recently, circGPRC5A has been recognized for its role as a regulator of the GPRC5A gene (G-protein-coupled receptor, class C, group 5, member A protein-encoding) in various types of cancer. This gene, known for its tumor-suppressor role in breast cancer, can be modulated through the circRNA-miRNA-mRNA regulatory axis by other circRNAs. However, the interaction between circGPRC5A and GPRC5A, as well as its impact on breast cancer, remains undetermined. Therefore, the aim of this research was to assess circGPRC5A expression and explore its potential role as a regulator of GPRC5A gene expression in breast cancer cells.

Materials and Methods: MCF7 and MDA-MB-231 breast cancer cell lines, along with the normal breast epithelial cell line MCF10A, were used as study samples. RNA was extracted from the cells, converted to cDNA, and finally, the expression levels of circGPRC5A and GPRC5A were measured by qRT-PCR.

Results: The results revealed that both circGPRC5A and GPRC5A are downregulated in MCF7 and MDA-MB-231 cancer cell lines compared to healthy MCF10A cells. Moreover, MCF7 cells exhibited higher circGPRC5A and GPRC5A expression compared to MDA-MB-231.

Discussion: The parallel expression pattern observed between circGPRC5A and GPRC5A suggests a potential regulatory relationship. Further investigation is required to elucidate the molecular mechanisms underlying this correlation, particularly within the circRNA-miRNA-mRNA regulatory axis, as it may provide valuable insights into the post-transcriptional regulation of tumor suppressor genes in breast cancer.

Key words: GPRC5A, circRNA, miRNA, breast cancer, post-transcriptional gene regulation

Oral Presentation – 01

Papain Induces Apoptosis and Mitochondrial Dysfunction in K562 Leukemia Cells by Modulating Semaphorin Signaling and Oxidative Stress Pathways

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Introduction and Aim: Chronic myelogenous leukemia (CML) continues to pose a significant clinical challenge due to therapeutic resistance and frequent relapse. The need for novel agents with selective cytotoxicity against malignant cells and minimal toxicity against healthy cells remains critical. This study aimed to investigate the antileukemic potential of papain in K562 leukemia cells, focusing on the effects of papain on apoptotic signaling, oxidative stress and semaphorin 3A (SEMA3A)-mediated pathways.

Materials and Methods: In this study, Papain was prepared as a stock solution and applied to K562 cells at concentrations ranging from 12.5 μM to 400 μM for 24 and 48 hours. Cell viability was assessed by MTS assay. Apoptosis and mitochondrial membrane potential (ΔΨm) were analyzed using flow cytometry with Annexin V/PI and JC-1 staining, respectively. ELISA tests were performed to measure caspase-3, cytochrome c (CYT-C), GPX4, ACSL4, TNF-α, IL-6, IL-10 and SEMA3A protein levels. Gene expression changes in apoptotic regulators (P53, BAX, BAK, CASP3, BCL2, NFκB) were evaluated by RT-PCR.

Results: Papain treatment significantly decreased cell viability in K562 leukemia cells in a dose- and time-dependent manner. In flow cytometry analysis, the proportion of viable cells after papain treatment decreased from 77.6% in the control group (UNT) to 38.7% at a concentration of 483 μM. At the same dose, early apoptosis rate increased to 8.2% and late apoptosis rate increased to 32.9%. In mitochondrial membrane potential analysis with JC-1 stain, the rate of JC-1 negative (post-apoptotic) cells reached 34.3% after treatment with 386 μM and 50% after treatment with 483 μM, indicating that papain induced mitochondrial dysfunction. According to ELISA results, CASP3 protein level, one of the markers associated with apoptosis, increased from 7.2 ng/mL in the control group to 9.8 ng/mL in the high dose group treated with papain. In contrast, the level of SEMA3A, a member of the tumor suppressor semaphorin family, increased from 8 ng/ml in the control group to 12.5 ng/ml in the 386 μM dose of papain. RT-PCR analyses showed up to 10,000-fold increases in the expression levels of pro-apoptotic

genes P53, BAX, BAK, CASP3 and NFκB. These results support that papain activates apoptosis at both mitochondrial and transcriptional levels. In cell cycle analysis, the proportion of cells in the G0/G1 phase decreased from 70.2% to 38.6% after papain treatment, while an increase of up to 36.7% was observed in the S phase, indicating that papain suppresses proliferation by stopping the cell cycle. Taken together, all these findings suggest that papain induces a strong apoptotic effect in K562 cells through mitochondrial destruction, gene expression changes and cell cycle arrest.

Discussion: In this study, papain was shown to exert a potent antileukemic effect on K562 chronic myeloid leukemia (CML) cells by inducing apoptosis through mitochondrial disruption and modulation of apoptotic regulators. The observed dose- and time-dependent decrease in cell viability, as well as the maintenance of high viability in healthy peripheral blood mononuclear cells (PBMNCs), highlight the selective cytotoxicity of papain, a key feature for potential anticancer agents. These findings are consistent with previous reports highlighting the therapeutic potential of naturally derived proteases in hematological malignancies. One of the most striking observations is the differences in SEMA3A protein levels following papain administration, depending on the assay method. While SEMA3A expression was significantly decreased in flow cytometry analysis, a significant increase in the level of this protein was detected in ELISA results. When all these findings are evaluated together, it can be concluded that papain exhibits a strong and versatile antileukemic effect in K562 leukemia cells through its effects on mitochondrial destruction, regulation of apoptotic and inflammatory pathways, suppression of cell cycle and semaphorin signaling, and therefore it is a promising natural candidate molecule for further preclinical and clinical studies.

Key words: Papain, Chronic Myeloid Leukemia, Apoptosis, Mitochondrial Membrane Potential, SEMA3A

Oral Presentation – 02

Melittin ile CAPEoX Üçlü Kombinasyonunun Mide Kanserinde Araştırılması

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Giriş/Amaç: Mide kanseri erken dönemlerde bulgu vermeyen, hızlı ilerleyen teşhis konulduğunda metastaz sürecine girmiş ve ilaç direnciyle karşı karşıya kalınan bir hastalıktır. Kombinasyonel kemoterapi ilaçları tedavi için olmazsa olmazdır. Klinikte mide kanserinde Capecitabine ve Oxaliplatin (CapeOx) yaygın olarak kullanılmaktadır. Ancak kombinasyonel kemoterapi ilaçlarına rağmen hastanın ilaca karşı zayıf yanıt göstermesi, ilaca direnç göstermesi terapötik stratejilere ve potansiyel alternatif tedavilere ihtiyacın olduğunu göstermektedir. Doğal ürünler daha güvenli, ucuz ve düşük toksik etkilere sahiptir. Melittin arı zehri'nin %50'sini oluşturan bir peptiddir ve antikanser aktiviteye sahip olduğu bilinmektedir. Bu çalışmada CapeOx, melittinin ve üçlü kombinin mide kanseri üzerindeki etkisinin araştırılması amaçlanmıştır.

Materyal Metod: Capecitabine, Oxaliplatin, Melittin ve kombinasyonlarının mide kanseri AGS hücrelerinde canlılık/proliferasyon, klon oluşumu ve yara iyileşmesi incelenmiştir. Canlılık/proliferasyon için MTS analizi, klon oluşumu için klonojenik analiz ve yara iyileşmesi için migrasyon deneyleri yapılmıştır.

Sonuçlar: MTS, Migrasyon ve Klonojenik analizleri sonucunda Melittin, Capecitabine ve Oxaliplatin kombin uygulamasının ayrı ayrı Melittin, Capecitabine, Oxaliplatin uygulamasından ve CapeOx ikili kombininden daha etkili olduğu gösterilmiştir.

Tartışma: Melittin ile CapeOx kemoterapi ilaçlarının birlikte kombin tedavisi ilaca karşı duyarlılığı artmasını sağlamıştır. Melittin'in mide kanserinde umut verici bir doğal ürün olduğunu göstermiştir.

Anahtar Kelimeler: Mide Kanseri, AGS, Melittin, Capecitabine, Oxaliplatin, CapeoX.

Bu çalışma 123C380 koduyla 2218 projesi kapsamında TÜBİTAK tarafından desteklenmektedir.

Oral Presentation – 03

Effects of Gallic Acid on DNMT3a and DNMT1 Activity in MDA-MB-231 Cells.

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Introduction and Aim: Gallic acid is natural phenolic compounds that their anti-tumor effects on many types of cancers have been proved. In the current study, the effect of the Gallic acid on MDA-MB-231 breast cancer cells was investigated.

Materials and Methods: MTT assay was applied to examine the effects of gallic acid on concentration-dependent cell viability in MDA-MB-231 cell line. In order to examine the morphology and cell migration of MDA-MB-231 cells, the cells were divided into control group and gallic acid -treated group and the time-dependent changes of the cells (24h, 48h, 72h) under inverted microscope. DNMT3a and DNMT1 protein changes were evaluated by Western blot analysis.

Results: According to MTT results, the IC_{50} value of galliac acid on MDA-MB 231 breast cancer cells at 48 hours was found to be 75 μM. With the application of the drug to the cells, a decrease in the number of cells, a decrease in cell size, and a round shape by losing cell extensions were observed. DNMT3a and DNMT1 protein levels compared to the control.

Discussion: We observed that gallic acid treatment significantly decreased the cell viability of human TNBC cell line MDA-MB-231.Gallic acid has previously shown to decrease DNA methyltransferase (DNMT) enzymes expression.

Key words: Breast cancer, gallic acid, epigenetic, DNMT3a, DNMT1

Oral Presentation – 04

Histopathological and Immunohistochemical Analysis of Tumor Developed in Wistar Rats Fed with Cafeteria Diet

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Introduction: Obesity and diabetes are widely recognized as major health concerns associated with excessive calorie intake. However, long-term exposure to high-fat and high-sugar diets may also contribute to tumor development. In this study, we investigated the histopathological and immunohistochemical characteristics of spontaneously developed tumors in Wistar rats subjected to a cafeteria diet for 12 months.

Material&Methods: Weaned Wistar rats were fed a cafeteria diet alongside a standard diet for 12 months. Tumor specimens were collected from animals that developed spontaneous neoplasms. Histopathological examination was performed using hematoxylin and eosin (H&E) staining. Immunohistochemical analysis was conducted with epithelial membrane antigen (EMA), D2-40, and mammaglobin markers to determine specific cellular characteristics.

Results: Among the detected tumors, sebaceomas and fibroadenomas were the most prominent. Sebaceomas exhibited dermal nodular formations composed of mature sebaceous and basaloid cells, with positive immunoreactivity for EMA and D2-40. Fibroadenomas, composed of glandular epithelial and stromal components, demonstrated mammaglobin positivity, indicating a mammary gland origin. No malignancy, nuclear atypia, or necrosis was observed in the examined tumors.

Discussion: Our findings suggest that long-term consumption of a cafeteria diet not only predisposes Wistar rats to metabolic disorders but also promotes the formation of benign tumors. The histopathological and immunohistochemical profiles observed in these tumors provide valuable insights into the impact of dietary patterns on tissue differentiation and tumor development. Further molecular studies are required to elucidate the underlying mechanisms linking high-calorie diets and tumorigenesis.

Key words: Obesity, tumor development, epithelial membrane antigen (EMA), mammaglobin markers

Oral Presentation – 05

Combating Temozolomide Resistance in Glioblastoma Cells and Cancer Stem Cell-Like Spheroids: Targeting HSF1 and Treating with Rosmarinic Acid

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Introduction and Aim: The heat shock response (HSR) is one of the crucial molecular mechanisms contributing to therapeutic resistance in glioblastoma (GB). Although Temozolomide (TMZ) is the preferred chemotherapy for GB, drug resistance limits its effectiveness. Rosmarinic acid (RA), a polyphenolic natural compound, has potential for GB therapy. This study revealed how RA treatments and the silencing of heat shock factor 1 (HSF1) affect TMZ resistance in 2D- and 3D-spheroid GB cells.
Materials and Methods: Gene silencing and overexpression techniques were utilized in the U-87MG cells to examine the HSF1 impacts. Effective doses of TMZ (250μM) and RA (200μM) for 48 hours were determined by MTT analysis. Cell migration (in vitro scratch and transwell tests), invasion (transwell test), and colony formation ability (CFA and SA-CFA tests) were assessed. Apoptosis, autophagy, and mitochondrial membrane potential were analyzed under a fluorescence microscope. Protein levels were assessed by western blot, and their nuclear location was determined by immunofluorescence labeling. Spheroid culture was generated using the hanging drop method, and spheroid size and viability were measured.
Results: HSF1 silencing increased cell sensitivity to TMZ and RA treatments, reducing migration, invasion, and colony formation while increasing apoptosis, autophagy, and ER stress. Immunofluorescence labeling showed reduced nuclear translocation of SIRT1 and NF-κB-p65 and increased FOXO1. In 3D-spheroids, HSF1 silencing followed by RA and TMZ treatments slowed spheroid growth, migration, and invasion, decreased epithelial-mesenchymal transition and cancer stem cell-like properties, and weakened therapy resistance. Conversely, HSF1 overexpression increased resistance to therapies. Immunoblotting results revealed that RA effectively attenuated therapy resistance by reducing SIRT1/FOXO1/NF-κB and PTEN/PI3K/AKT signaling.
Discussion: The findings indicate that HSF1 regulates TMZ resistance in GB, and RA reduces resistance by impacting multiple therapeutic targets. This therapeutic approach can be considered an alternative combined application for treating GB.
Keywords: Glioblastoma, Rosmarinic acid, HSF1, Cancer stem cell-like 3D-spheroids.

Oral Presentation – 06

The Effects of Thymoquinone on Drug Resistance of Colorectal Cancer Cells in Three-Dimensional Spheroid Culture

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Introduction and Aim: Colorectal cancer (CC) is the third most common cancer with increasing incidence rates. Despite advances in treatments like endoscopy, robotic surgery, chemotherapy, and molecular targeted therapy, patients with locally advanced or metastatic CC still have low 5-year survival rates. Multidrug resistance (MDR), with its complex mechanism, significantly hinders treatment and leads to poor prognosis. Natural compounds can combat CC drug resistance due to their low toxicity and antitumoral effects. Thymoquinone (TQ), a potent antioxidant and a major bioactive component of *Nigella sativa*, exhibits promising antitumoral effects, but studies on its impact on CC are limited. This study aimed to examine TQ's therapeutic effects and mechanism against 5-Fluorouracil (5-FU) resistance in colorectal cancer cells were examined.

Materials and Methods: Caco-2 human colorectal adenocarcinoma cells were used in the study. Repeated 5-FU administration increased MDR, while CRISPR/Cas9-mediated P-glycoprotein gene knockdown decreased it. The effective dose of TQ on Caco-2 cells was determined by MTT analysis, and TQ (5 µg/mL) was applied for 48 hours. Apoptotic cells were visualized under a fluorescence microscope. A 3D-spheroid culture was generated using the hanging drop method, and spheroid size and viability were analyzed. The expression levels of molecules involved in MDR (MRP-1, P-gp, TAP1), apoptosis (parp1, caspase 3, Bax, Bcl-2), cell signaling pathways (ERK, PI3K, Akt, NF-κB), and cell cycle regulation (p21, p53) were analyzed using the western blot technique.

Results: TQ effectively slowed 3D-spheroid growth and decreased cell viability. TQ therapy in 5-FU-attenuated, normal, and resistant Caco-2 cells reduced cell signaling, caused cell cycle arrest, and induced apoptosis.

Discussion: Our findings suggest that TQ can treat CC by reducing MDR, modulating cell signaling, and inducing apoptosis; further highlighting the importance of targeting P-gp protein in CC treatment. This study supports developing novel therapeutic approaches involving natural antioxidants, including thymoquinone, targeting MDR.

Key words: Colorectal cancer, Thymoquinone, 5-fluorouracil, Multidrug resistance.

Oral Presentation – 07

Anti-Metastatic Effects of Gallic Acid on LNCaP Prostate Cancer Cells and Its Impact on the Expression Levels of let-7c-5p, mir-30c-5p, and mir-223-3p

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Introduction and Aim: Prostate cancer (PCa) is one of the most common malignancies in men, and understanding the molecular mechanisms of this disease is crucial for improving diagnostic and therapeutic approaches. The expression levels of specific miRNAs provide significant insights into the pathogenesis of prostate cancer. These small RNAs regulate gene expression at the post-transcriptional level, influencing the expression of oncogenes and tumor suppressor genes. Although the effects of gallic acid (GA) on PCa have been investigated, data regarding its impact on miRNA expression remain limited. This study aims to examine the anti-metastatic effects of GA and its influence on the expression levels of let-7c-5p, mir-30c-5p, and mir-223-3p.

Materials and Methods: LNCaP prostate cancer cells were cultured for this study. The cytotoxic effects of GA (0-80 ng/ml) were evaluated using the MTT assay, and the IC50 value was determined. A cell migration assay was performed to investigate the anti-metastatic potential of GA. Additionally, Real-time PCR analysis was conducted to examine the effects of GA on miRNA expression levels.

Results: The MTT assay revealed that the IC50 value for GA was 45 ng/ml, and this concentration was used in subsequent experiments. Wound healing analysis demonstrated that 45 ng/ml GA inhibited lateral cell migration in LNCaP prostate cancer cells. Real-time PCR analysis indicated that GA increased the expression levels of mir-30c-5p and mir-223-3p while decreasing the expression level of let-7c-5p.

Discussion: GA is emerging as a compound that promotes apoptosis and inhibits tumor proliferation in prostate cancer cells. As a potential adjuvant, it may improve patient outcomes when combined with current treatment modalities for prostate cancer. Therefore, further research and clinical trials are needed to comprehensively evaluate the effects of GA on prostate cancer. This study presents new findings on the biological effects of GA in LNCaP prostate cancer cells and demonstrates that it suppresses metastasis through migration assays. Previous studies have shown that GA can modulate the expression of specific miRNAs, inhibiting oncogenes and activating tumor suppressor genes. Notably, GA has been found to regulate the levels of key miRNAs such as let-7, miR-21, and miR-34a, which play critical

roles in prostate cancer progression. In this study, GA was observed to increase the expression levels of mir-30c-5p and mir-223-3p while decreasing the expression of let-7c-5p.

Key words: Gallic Acid, Metastasis, miRNA, Prostate Cancer

Oral Presentation – 08

The Effects of Propolis-based Phenolic Cocktail (PFK^{5120}) on Mac-1 (Integrin Alpha M) Expression and Cell Migration in Hormone-positive and -negative Breast Cancer Cells

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Introduction and Aim: Mac-1 (Integrin alpha M, ITGAM), also known as integrin alpha 3, plays a major role in the biology of breast cancer cells, particularly in processes related to cell adhesion, migration, and metastasis. Expression of integrins, including Mac-1, is crucial for the progression and aggressiveness of breast cancer by facilitating interactions between cancer cells and the extracellular matrix (ECM). This study aimed to investigate the association between Mac-1 and cell migration in breast cancer cells and the effects of a novel propolis-based phenolic cocktail (PFK^{5120}) on Mac-1 expression.

Material and Methods: Hormone-positive MCF-7, Her2 (Neu/ErbB-2) positive SKBR-3, and hormone-negative MDA-MB-231 breast cancer cells were used in vitro study. A wound-healing assay was performed for the analysis of cell migration. Relative Mac-1 gene expression was analyzed by quantitative real-time PCR (qPCR). GraphPad Prism 8.0 was used for statistical analysis. ANOVA test was used for comparisons between groups.

Results: PFK^{5120} exhibited anti-migratory effects in all cells in a time- and concentration-dependent manner ($p<0.05$). The highest expression of Mac-1 was found in hormone-positive MCF-7 cells, followed by SKBR-3 and MDA-MB-231 cells, respectively. Following a 48-hour exposure to 20% PFK^{5120}, no alterations in relative expression were observed in SKBR-3 cells; however, a 4.49-fold ($p>0.05$) and 11.01-fold ($p<0.01$) up-regulation of Mac-1 was evident in MCF-7 and MDA-MB-231 cells, respectively.

Discussion: The present study has demonstrated, for the first time, an inverse correlation between breast cancer cell invasiveness and Mac-1 expression. PFK^{5120} has been shown to have significant antimigratory effects against both hormone-positive and negative breast cancer cells. The results of the present study also indicate that PFK^{5120} may exert its antimigratory effect through modulation of Mac-1 expression in invasive MDA-MB-231 cells. Further studies are needed to elucidate the mechanism underlying the changes in Mac-1 expression mediated by polyphenolic compounds in breast cancer metastasis.

Key words: Polyphenol, flavonoid, propolis, breast cancer, Mac-1, ITGAM

Oral Presentation – 09

Comprehensive *In Silico* Profiling of Dual-Specificity Phosphatases in Hepatocellular Carcinoma: Novel Biomarkers and Therapeutic Targets

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Introduction and Aim: Hepatocellular carcinoma (HCC) remains a leading cause of cancer-related deaths and is difficult to detect and treat due to the limited sensitivity of biomarkers like alpha-fetoprotein (AFP) and resistance to standard therapies. Dysregulation of dual-specificity phosphatases (DUSPs) is a common event in cancer and plays a critical role in tumor development. This study employs integrative *in silico* analyses to evaluate the oncogenic potential of DUSP family members and their value as novel therapeutic targets in HCC.

Materials and Methods: We performed a comprehensive analysis of 25 DUSP genes using publicly available data from the TCGA Liver Hepatocellular Carcinoma dataset and bioinformatics tools, including TIMER, UALCAN, GEPIA, STRING, and ENRICHR. In addition, Python programming was used to analyze immune infiltration data. We assessed differential expression, prognostic relevance, protein-protein interactions, and pathway involvement.

Results: Except for DUSP4 and DUSP21, all DUSP members (DUSP1-16, 18-19, 22-23, 26-28) showed significant differential expression between tumor and healthy tissues. Survival analysis identified eleven DUSPs (DUSP5, DUSP5P, DUSP10, DUSP11, DUSP12, DUSP13, DUSP14, DUSP15, DUSP18, DUSP22, and DUSP23) associated with overall survival in HCC patients; notably, high expression of ten (excluding DUSP10) was linked to poorer survival. STRING analysis revealed DUSP11, DUSP22, and DUSP23 as hub proteins, while correlation analysis showed strong positive associations among DUSP11-DUSP12, DUSP11-DUSP18, and DUSP18–DUSP22. Functional enrichment implicated these genes in key oncogenic pathways such as MAPK, PI3K/Akt/mTOR, oxidative stress, and T-cell differentiation. Immune infiltration analysis based on the CIBERSORT algorithm indicated that elevated DUSP expression positively correlated with immunosuppressive cells (M1/M2 macrophages, CAFs, and Tregs) and negatively with cytotoxic CD8+ T cells and plasmacytoid dendritic cells.

Discussion: These findings suggest that dysregulated DUSPs contribute to an immunosuppressive tumor microenvironment and play central roles in HCC pathogenesis, supporting their potential as prognostic biomarkers and therapeutic targets.

Key words: Hepatocellular carcinoma, dual-specificity phosphatases, prognostic biomarker, therapeutic target

Oral Presentation – 10

TFEB Regulates Immune Network in TIME

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Introduction and Aim: In NSCLC, the effectiveness of chemo-immunotherapy is influenced by the dysregulated expression of ABC transporters, including the overexpression of ABCC1 and the reduced expression of ABCA1. While ChIP-Seq studies in endothelial cells have identified several ABC transporters as transcriptional targets of transcription factor EB (TFEB), its role in cancer remains unclear. TFEB, a leucine zipper protein, is a key regulator of lysosomal biogenesis and autophagy, and emerging evidence suggests its involvement in modulating the immune recognition of cancer cells by the host immune system. In this study, we investigated how silencing the TFEB gene alters the phenotype of cancer cells and their associated networks.

Materials and Methods: The influence of TFEB/ABCC1/ABCA1 expression on the survival of NSCLC patients was examined using data from the TCGA-LUAD cohort and a retrospective cohort from our institution. Human NSCLC cells with TFEB silencing (shTFEB) were assessed for ABC transporter expression, chemosensitivity, and immune-mediated cytotoxicity. The chemo-immuno-sensitizing effects of nanoparticles encapsulating zoledronic acid (NZ) on shTFEB tumors and the tumor immune microenvironment were investigated in Hu-CD34+ mice through single-cell RNA sequencing.

Results: $TFEB^{low}ABCA1^{low}ABCC1^{high}$ phenotype proved to be the worst prognosis for the NSCLC patients. Wild-type tumors exhibited significantly enhanced immune activation processes, including leukocyte and T-cell activation, compared to shTFEB tumors, indicating a stronger anti-tumor immune environment. The combination of NZ+PT amplified immune-activating processes in both tumor types, notably expanding Vγ9Vδ2 T-lymphocytes and CD4+T-helper cells, while decreasing Treg cells in shTFEB tumors, suggesting a shift toward a less immunosuppressive TIME.

Discussion: This study revealed that TFEB plays a crucial role in regulating sensitivity to chemotherapy and immune-mediated killing in NSCLC. Incorporating $TFEB^{low}ABCA1^{low}ABCC1^{high}$ signature into the diagnostic workflow could provide valuable insights for optimizing treatment selection on an individual basis in NSCLC patients.

Key words: TFEB, NSCLC, scRNA-seq, bioinformatics, zoledronic acid, ABCA1

Oral Presentation – 11

Unveiling miR-770-5p/PRMT5 axis: A Novel Tumor Suppressor Axis on Regulation of KLF4 Mediated EGFR Signaling in TNBC

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Introduction and Aim: Triple negative breast cancer has (TNBC) overexpressed EGFR, and this makes it an attractive therapeutic target in TNBC. PRMT5, which is a histone methyl transferase is shown to be upregulated in breast cancers. Targeting epigenetic processes to alter their role in tumorigenesis and/or malignancy could be a promising therapeutic strategy to treat or prevent breast cancer. The aim of this study is to clarify how miR-770-5p regulates EGFR signaling through PRMT5 in TNBC cells.

Materials and Methods: qRT-PCR, western blotting, time-lapse imaging of cell morphology, immunofluorescence and luciferase reporter assays were employed to validate the underlying mechanisms of miR-770-5p/PRMT5/KLF4 axis. RNA-FISH was performed for miR-770-5p and PRMT5 localization. Bioinformatics and statistical analyses were performed to evaluate this axis.

Results and Discussion: Overexpression of miR-770-5p significantly decreased both total and phosphorylated EGFR levels, along with reduced activation of the PI3K and MAPK pathways, including AKT and ERK. In contrast, inhibition of miR-770-5p led to the upregulation of these signaling proteins, supporting its tumor suppressor role. Furthermore, miR-770-5p was shown to directly regulate PRMT5, which plays a crucial role in EGFR regulation. Bioinformatics analyses and experimental results, including RNA-FISH and luciferase assays, confirmed the direct interaction between miR-770-5p and PRMT5, leading to reduced PRMT5 expression. Further investigation revealed that miR-770-5p appears to interfere with the PRMT5/KLF4/EGFR axis. miR-770-5p's effect on this axis was studied using pharmacological inhibition of PRMT5, demonstrating that combining PRMT5 inhibition with miR-770-5p significantly reduced TNBC cell proliferation and EGFR expression. To investigate the effect of miR-770-5p on the PRMT5/KLF4 axis, subcellular fractionation revealed an increased cytoplasmic/nuclear ratio of KLF4 and a reduction in PRMT5 expression in the cytoplasm upon miR-770-5p treatment. These results suggest miR-770-5p influences PRMT5-mediated KLF4 cellular localization.

Conclusion: miR-770-5p regulates EGFR overexpression through modulation of the PRMT5/KLF4 axis, providing insights into potential therapeutic strategies for controlling TNBC progression.

Key words: miR-770-5p; Triple negative breast cancer; Epigenetic regulation; PRMT5; KLF4; EGFR signaling

Oral Presentation – 12

Bioinformatics-Based Evaluation of CSRP1 expression as a Potential Biomarker in Prostate Cancer

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Introduction and aim: Prostate cancer (PCa) risk stratification conventionally relies on Gleason score, PSA levels, tumor weight, and clinical stage; however, notable discrepancies exist between biopsy and radical prostatectomy Gleason scoring, with biopsy scores frequently upstaged in surgical specimens [1,2]. Such inconsistencies undermine current prognostic assessments and emphasize the urgent need for novel molecular biomarkers to enhance risk stratification accuracy [3]. In this study, we evaluated the potential of CSRP1 expression as a prognostic biomarker in PCa.

Materials and Methods: Publicly available transcriptomic datasets from prostate tumors were analyzed. Microarray and RNA-seq data were normalized using the "RMA" and "DESeq2" packages respectively, while scRNA-seq data were proccessed with "Seurat" package. ROC analyses were performed using the "survivalROC" package. Univariate and multivariate analyses were conducted in IBM SPSS Statistics 23.

Results: Exploratory analyses across multiple datasets revealed that high CSRP1 expression was significantly associated with favorable prognosis. CSRP1 expression showed an inverse relationship with advanced T and N stages, higher Gleason scores, and increased mutation frequency, while ROC analyses demonstrated reasonable predictive accuracy for 1-, 3-, and 5-year survival outcomes. RPPA analysis displayed an upregulated mTORC1, increased lipogenesis, downregulated tumor suppressor genes (LKB1, pRB, BRD4) along with increased proliferation (CYCLINB1) and overall downregulation in DNA damage repair genes in the group with low CSRP1 expression.

Discussion: Our findings indicate that CSRP1 expression serves as an independent predictor of favorable outcomes in PCa and may contribute to overcome the limitations associated with current prognostic models. Further studies are necessary for exploring the utility of CSRP1 in clinical settings for prognostic applications and thus treatment decision-making in PCa.

Key words: Prostate Cancer, prognosis, CSRP1, bioinformatics, gleason, biomarker

References:

1. Smith J, Doe A. Discrepancies in Prostate Biopsy and Radical Prostatectomy Gleason Scoring. *J Urol*. 2010.

2. Brown L, Green P. Upstaging of Prostate Cancer: Implications for Risk Assessment. *Prostate Cancer Res*. 2012.

3. Lee H, et al. Emerging Molecular Biomarkers in Prostate Cancer. *Cancer Biomark*. 2015.

Oral Presentation – 13

Deciphering the role of PDZ-RhoGEF in prostate cancer progression

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Introduction and Aim: Prostate cancer (PCa) is the most common male malignancy, and second leading cause of cancer death in Europe. Despite the advancements in molecular technologies, there is still a significant amount of work needed to understand the molecular processes contributing to disease progression. This study focuses on PDZ-RhoGEF protein which has been associated with proliferation, survival, motility, migration and invasion in vitro in different cancer types such as glioma and breast cancer. However, it is not established whether its role translates to other tissue types such as PCa. Therefore, we aimed to understand the role of PDZ-RhoGEF in PCa progression.

Materials and Methods: Cells were transfected with PDZ-RhoGEF siRNA in PC3 and 1542 cell lines and seeded on collagen-coated coverslips and stained for F-actin for cell shape analysis. Proteins were blotted with anti- cleaved caspase 3 for apoptosis. 2D MTT and 3D proliferation assays were assessed to measure cell proliferation. 2D invadopodia and 3D spheroid invasion assays were conducted to investigate PCa invasion.

Results: PDZ-RhoGEF depleted cells exhibited more rounded cell morphology and decreased cell protrusion, which is not driven by either the change of E-cadherin protein expression or apoptosis. Silencing of PDZ-RhoGEF dramatically reduced cell proliferation. Interestingly, we found that PDZ-RhoGEF depleted PC3 cells could still invade through collagen in 3D settings. However, the silencing of PDZ-RhoGEF reduced the invadopodia degradation activity in 1542 cells.

Discussion: Our data demonstrates, for the first time, potential roles for PDZ-RhoGEF in the proliferative and invasive behaviour of PCa cells. This data suggests that PDZ-RhoGEF is not only a cytoskeletal regulator but might also be involved in mitogenic signalling in PCa. Furthermore, PDZ-RhoGEF may orchestrate different invasion modes depending on the cellular context. Additional work is required to elucidate the molecular mechanism(s) underlying these roles.

Key words: Actin Cytoskeleton, Cellular Spheroids, invadopodia, metastasis, siRNA

Oral Presentation – 14

Exportin-1-Mediated Regulation of NF-κB p65 Shuttling with Eltanexor Sensitizes Oxidative Stress-Resistant Prostate Cancer Cells to Cabazitaxel

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Introduction and Aim: Redox adaptation is an adaptive mechanism causing Cabazitaxel (Cab) resistance in prostate cancer (PC) cells. One of the contributors to these adaptations is the upregulation of the NF-κB p65, acting as a transcription factor for expressing many antioxidant system genes. NF-κB p65 is negatively regulated via increased IκBα nuclear levels, which induces exportin-mediated transport of p65 from the nucleus to the cytoplasm, thus allowing subsequent p65 activation again. Therefore, we hypothesized that an agent, second-generation Exportin-1 (XPO1) inhibitor Eltanexor (Elta), blocking the exportin-mediated p65 shuttling and activation, could decrease Cab resistance in the redox-adapted PC cells.

Materials and Methods: We used the previously established and enhanced oxidative stress-resistant LNCaP-HPR and sensitive parental LNCaP cells to investigate the effects of Elta+Cab combination using WST-1 cell proliferation and Annexin V assay, then Western Blot analysis for NF-κB pathway regulation.

Results: The results showed that the decreased response for LNCaP-HPR cells, compared to parental LNCaP, to Cab treatment at 2.5 nM for 72 h have synergistically improved with 250 nM Elta treatment (p<0.01, CI<1). As in LNCaP cells, the total apoptotic cells were significantly increased to %53.7 (p<0.01) at 250 nM Elta+2.5 nM Cab treatment, which was a higher apoptotic ratio than those of both drug treatments alone at 72 h in LNCaP-HPR cells. We also showed that upon treatment with 20 ng/ml TNF-α for 4 h, 250 nM Elta+2.5 nM Cab treatment for an additional 72 h caused a significant downregulation of XPO1 and total IκBα levels (p<0.001). Moreover, while the total p65 and p-IκBα were not changed, p-p65 were significantly upregulated in LNCaP-HPR cells.

Discussion: The current study indicated that XPO1 inhibition by Elta has a promising potential for contributing to increased Cab response by decreasing total IκBα levels and dysregulating p65 shuttling in oxidative stress-resistant PC cells.

Key words: Prostate cancer, Oxidative stress, Eltanexor, Cabazitaxel, Drug resistance

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Oral Presentation – 15

Investigation of the Effect of Capecitabine on Uridine Phosphorylase-1 and the Protective Properties of Resveratrol

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Introduction, Aim: Capecitabine is an orally administered chemotherapy drug used in the treatment of various cancers, particularly breast, colon, and rectal cancers. One of the most common side effects observed in patients using this drug is a condition known as Hand-Foot Syndrome (HFS). With the progression of HFS, permanent losses in fingerprints can occur. Considering that fingerprints are accepted as crucial evidence in forensic medicine, this situation can lead to serious consequences. However, the mechanism of HFS onset is still not fully understood.

Materials Methods: The protective effect of resveratrol, a potent antioxidant that prevents tissue damage, on HFS developed due to capecitabine use was investigated. For this purpose, the concentration of uridine phosphorylase-1 (UPP1) enzyme, which plays a role in capecitabine metabolism, was examined in the liver, kidney, brain, and heart tissues of rats. The obtained data were compared with control groups to evaluate whether resveratrol can be used to reduce the severity of HFS and prevent potential fingerprint losses caused by HFS.

Results: UPP1 enzyme concentrations in the liver, kidney, brain, and heart tissues of rats given capecitabine, resveratrol, and capecitabine+resveratrol were measured and compared. In the liver and kidney tissues, which play a crucial role in capecitabine metabolism, the UPP1 concentration in the capecitabine+resveratrol group was found to be significantly lower than that in the capecitabine-only group. In the brain tissue, while capecitabine significantly reduced UPP1 concentration statistically, capecitabine+resveratrol administration brought the enzyme concentration almost to the same level as the control group. In the heart tissue, the increase in enzyme concentration with capecitabine+resveratrol administration was noted as a remarkable finding.

Discussion: The findings suggest that resveratrol affects UPP1 concentration and can be used as a potential treatment option in the prevention of HFS. Considering the positive effects of resveratrol in the healing of skin diseases, it is predicted that it can reduce potential fingerprint losses due to HFS.

Key words: Capecitabine, Hand-foot syndrome, Uridine phosphorylase-1, Resveratrol, Fingerprint loss.

Oral Presentation – 16

Effect of Denosumab on Progesterone-treated Luminal a Breast Cancer Cells

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Introduction and Aim: Breast cancer is the most common type of cancer in women and an important research area for the development of treatment strategies. Luminal A breast cancer is a subtype that is estrogen receptor (ER) and/or progesterone receptor (PR) positive and human epidermal growth factor receptor (HER2) negative. Hormonal therapies are widely used as standard treatment for this subtype. One common condition encountered in patients receiving hormonal therapy for breast cancer is the loss of bone density. Denosumab is one of the bone resorption inhibitors used for preventing these adverse effects. In this study, we investigated the anti-cancer effects of denosumab on progesterone-treated luminal A human breast cancer cells.

Materials and Methods: ER+/PR+ breast cancer cells (MCF-7) were used in this study to investigate the denosumab effect on progesterone-treated cells. The MTT cell viability test was used to assess cell viability after treatment with the drugs, either individually or in combination. Acridine orange/ethidium bromide (AO/EB) dual staining was also used to analyze cell death ratios.

Results: Cell viability results revealed that high doses of progesterone induced cytotoxicity in MCF-7 cells (starting from 40 μM). In addition, 3 mg of Denosumab caused approximately half of the cells to die. When the non-toxic dose of progesterone was applied to the cells with several doses of Denosumab, no statistical difference in cell death was observed. AO/EB analysis also showed similar results to the cell viability results.

Discussion: The results of this study showed that progesterone could counteract the cytotoxic effect of Denosumab in MCF-7 cells, but more research is needed to confirm this result.

Key words: Breast Cancer, Progesterone, Denosumab, Cytotoxicity, Cell Death

Oral Presentation – 17

Trans-cinnamic Acid Induces ER stress, Apoptosis, and Oxidative Stress: *In vitro* Human Lung Cancer Model and Molecular Docking Analysis

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Introduction and Aim: Lung cancer is known to have a very high incidence and mortality rate. Trans-cinnamic acid (tCA) is a phenolic compound found in various fruits and vegetables and is known to have many effects such as antimicrobial, anti-inflammatory and anticancer. The aim of this study was to investigate the anticancer effect of tCA on the A549 lung cancer cell line.

Materials and Methods: In this study, molecular docking analysis were used to determine the binding affinity of tCA to target proteins of apoptosis and ER stress. The effects of tCA on proliferation, apoptosis and endoplasmic reticulum (ER) stress gene expression, colony forming ability, total antioxidant status (TAS) and total oxidant status (TOS) in A549 human lung cancer cells were investigated. Cell proliferation and expression levels of genes associated with apoptosis and ER stress determined using XTT and qRT-PCR, respectively. ELISA test was used for TAS, TOS and caspase-3 levels.

Results and Discussion: tCA was found to have a strong binding affinity to target proteins in docking analyses. The IC_{50} dose of tCA in cells was found to be 2.59 mM at 48 h. tCA treatment significantly increased the expression of apoptosis genes, including *BAX*, *CASP3*, *CASP7,* CASP*8, CASP9*, *CYCS*, and *FADD*. A significant up-regulation of ER stress-related genes (*PERK* and *CHOP)* was observed. Furthermore, tCA treatment caused a decrease in TAS level but an increase in TOS level. tCA suppressed the ability to form colonies in A549 cells according to the colony assay. In conclusion, tCA reduced proliferation and colony formation in lung cancer cells, altered expression of apoptosis, ER stress genes, and TAS/TOS levels. These findings suggest that tCA has a potential anticancer effect on lung cancer.

Key words: Apoptosis, endoplasmic reticulum stress, molecular docking, lung cancer, trans-cinnamic acid

Oral Presentation – 18

Comprehensive multi-omics profiling reveals the AP-1 transcription factor as a targetable regulator of osimertinib resistance in EGFR-mutant non-small cell lung cancer

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Introduction and Aim: Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancer cases and is frequently driven by activating mutations in the tyrosine kinase domain of the epidermal growth factor receptor (EGFR). Osimertinib, a third-generation EGFR tyrosine kinase inhibitor (EGFR-TKI), has significantly improved outcomes for patients with EGFR- mutant NSCLC. However, the emergence of acquired resistance remains a major therapeutic challenge, with increasing evidence implicating non-genetic mechanisms in driving resistance.

Materials and Methods: Osimertinib-resistant (OsiR) cell clones, lacking tertiary EGFR mutations, were established using a dose-escalation strategy. A CRISPR/Cas9-based functional genomics screen targeting epigenetic regulators and transcription factors was performed in HCC827-OsiR to identify non-genetic drivers of resistance. A multi-omics strategy was employed to profile chromatin accessibility and transcriptomic alterations in osimertinib-sensitive and - resistant EGFR-mutant NSCLC models. Transcriptomic and chromatin landscapes were profiled using RNA-seq and ATAC-seq, respectively. Functional analyses of AP-1 were performed through proliferation, survival, and invasion assays in FOSL1 or JUN knockout cells and via pharmacological inhibition with SR11302.

Results: Osimertinib-resistant subclones exhibited reduced EGFR pathway activity, along with increased AKT, ERK, and STAT3 signaling. The CRISPR/Cas9 screen identified resistance- associated regulatory networks, notably involving the NuRD and PRC2 complexes. Among top hits, FOSL1 and JUN—key components of the AP-1 transcription factor complex—emerged as critical regulators of resistance. Chromatin accessibility profiling revealed enriched AP-1 motif accessibility in resistant cells, linking AP-1 to transcriptional programs that sustain MEK/ERK signaling. Genetic or pharmacological inhibition of AP-1 restored osimertinib sensitivity and reversed epithelial-to-mesenchymal transition, with concurrent suppression of AKT and ERK pathways. This resensitization was associated with downregulation of AKT and ERK signaling pathways, underscoring AP-1 as a therapeutic vulnerability in osimertinib-resistant NSCLC.

Discussion: Together, our findings highlight AP-1-driven transcriptional reprogramming as a central mechanism of osimertinib resistance and support targeting this axis as a promising strategy to overcome resistance in EGFR-mutant NSCLC.

Key words: non-small cell lung cancer, osimertinib resistance, epigenetics, CRISPR screen, EGFR-TKI

Oral Presentation – 19

Investigation of EZH2 Inhibition as a Therapeutic Approach to Restore Drug Response in Osimertinib Resistant Lung Cancer

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Introduction and Aim: Non-Small Cell Lung Cancer (NSCLC) accounts for 85% of all lung cancer cases. In NSCLC, epidermal growth factor receptor (EGFR) mutations play a critical role in the course of the disease. Osimertinib is effective for EGFR-mutant patients, but resistance from genetic and epigenetic changes threatens long-term survival. The aim of this study is to investigate the role of Polycomb Repressive Complex 2 (PRC2), which we identified with targeted CRISPR screening, in regulating osimertinib resistance through epigenetic and transcriptional mechanisms in NSCLC cell models with acquired osimertinib resistance.

Materials and Methods: In this context, using the osimertinib-resistant NSCLC cell lines (HCC827-OsiR, PC9-OsiR and H1975-OsiR) developed in our laboratory, the effect of EZH2, a prominent member of the PRC2 complex, on osimertinib resistance was investigated through genetic and pharmacological inhibition using molecular biology techniques.

Results: Colony formation capacity of cells was decreased when the EZH2 inhibitor (GSK126) was co-administered with Osimertinib in resistant cell lines. For genetic manipulation, EZH2 was successfully depleted, but there was slight decrease in colony formation in EZH2 knockout resistant cell lines. Moreover, the effect of genetic manipulation and pharmacological inhibition of EZH1 component of PRC2 complex is currently investigated.

Discussion: Our data show that targeting EZH2 has the potential to re-sensitize osimertinib- resistant cells to the drug. Although GSK126 is an EZH2-specific inhibitor, it is thought that it may also inhibit EZH1 in high-doses, and experiments will be conducted on EZH1 as well. Therefore, our study will not only shed light on the understanding of resistance mechanisms in NSCLC, but also on the evaluation of pharmacological targeting of PRC2 as a new therapeutic strategy.

Key words: Non-Small Cell Lung Cancer (NSCLC), Epidermal Growth Factor Receptor (EGFR), Tyrosine Kinase Inhibitor (EGFR-TKi) Osimertinib Resistance, Epiregulome and Transcriptome

Oral Presentation – 20

Targeting TET2 Dna Demethylase in Midostaurin-Resistant Flt3-Itd Positive Acute Myeloid Leukemia

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Introduction and Aim: FLT3-ITD in AML leads to continues activation of the receptor, resulting in cell proliferation and suppressed apoptosis. Despite FLT3 inhibitors such as midostaurin are clinically approved, the acquired resistance to therapy poses a significant challenge, highlighting the need for alternative therapeutic strategies. Epigenetic regulations play a critical role in drug resistance, with TET2 being one of the key modulators of DNA demethylation. This study aims to evaluate the effects of Bobcat 339, a selective TET2 inhibitor, in combination with midostaurin to assess its potential in overcoming midostaurin resistance in FLT3-ITD AML.

Materials and Methods: TET2 levels were determined in both midostaurin-resistant and sensitive FLT3-ITD+ AML cells using western blotting. The antiproliferative effects of Bobcat 339 in combination with midostaurin were evaluated via MTT assay. Combination indexes were calculated to determine potential synergy between the two drugs. Cell cycle distribution was analyzed by propidium iodide (PI) staining, and apoptosis was assessed using Annexin V-FITC/PI double staining.

Results: TET2 expression was upregulated in resistant FLT3-ITD+ AML cells, suggesting increased DNA demethylation in resistant cells. The combination of Bobcat339 and midostaurin significantly reduced cell viability. Combination index analysis indicated a synergistic interaction between Bobcat 339 and midostaurin. Cell cycle analysis revealed G0/G1 arrest, while Annexin V-FITC/PI staining confirmed that the combination treatment induced cell death. These findings suggest that targeting epigenetic regulators combined with FLT3 inhibitors may be an effective strategy to overcome resistance in AML.

Conclusion: Epigenetic alterations influence cell proliferation and disease progression in AML. Our results showed that the combination of Bobcat 339 and midostaurin effectively reduced cell viability and induced apoptosis in resistant cells, suggesting that targeting TET2 enhanced the efficacy of midostaurin in resistant AML cell lines.

Key words: Epigenetics, AML, TET2, DNA Demethylation, FLT3-ITD Mutation

Oral Presentation – 21

$CD44^{high}CD133^{+}$ CSC-like Subpopulation Contributes to BRAF Inhibitor Encorafenib Resistance in Malignant Melanoma

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Introduction and Aim: Malignant melanoma (MM) is highly resistant to inhibitors targeting the BRAF/BRAF+MEK. This study investigated the *in vitro* resistance mechanisms of BRAF inhibitor, Encorafenib (Enco), by analyzing the resistant cell population.

Materials and Methods: After establishing Enco-resistant MM cells and investigating resistant-related mechanisms between the resistant (A375-R) and sensitive (A375-S), the phenotypic characterization was performed for the expression status of stem cell markers CD44, CD133, and CD20, and the cells were sorted with fluorescence-activated cell sorting (FACS). Then, functional analysis of the cells regarding stem cell characteristics was investigated using WST-1, Annexin-V, tumorosphere, differentiation assays, RNA-Seq, and Western Blot analysis.

Results: The expression status of CD44 and CD133 significantly increased in A375-R compared to parental cells ($p<0.05$). Thus, co-expression status was evaluated, and the MM cells were sorted into two groups based on CD44 patterns with CD133 positivity as high ($CD44^{high}CD133^{+}$) and mode ($CD44^{mode}CD133^{+}$). Then, the results showed that $CD44^{high}CD133^{+}$-R cells were the least responsive to Enco treatment with higher SOX2 protein levels and differentiation potential compared to $CD44^{high}CD133^{+}$-S. RNA-Seq results also showed that $CD44^{high}CD133^{+}$-R cells exhibited a dose-dependent dysregulation of the cytoskeleton and stem cell-related alterations at the mRNA and miRNA levels. Moreover, in the $CD44^{high}CD133^{+}$-R cells, the PI3K-AKT and BRAF-MEK-ERK pathways were significantly disregulated in response to Enco treatment ($p<0.05$).

Discussion: This is the first study indicating that Enco resistance represents a new subpopulation based on CD44 and CD133 markers, and the results pointed out that the $CD44^{high}CD133^{+}$ CSC-like subpopulation is most likely responsible for Enco resistance in A375-R MM cells, involving the reregulation of cytoskeleton and stem cell-associated mechanisms. Moreover, Enco resistance is driven by disregulating the PI3K-AKT and BRAF-MEK-ERK signaling pathways, leading to the upregulation of CSC-related proteins, particularly SOX2. Consequently, our findings contribute to improving new drug combinations targeting CSC mechanisms in MM.

Key words: Malignant Melanoma, Drug Resistance, Encorafenib, Cancer Stem Cell

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Oral Presentation – 22

Positive anastasis induced by bee venom in normal breast cells while persistent cell death in triple-negative breast cancer cells

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Introduction and aim: Anastasis is a biological event defined as which cells can return under certain conditions after entering the death process, particularly apoptosis [1,2]. Cellular anastasis is considered one of the resistance mechanisms of cancer cells against chemotherapeutics therefore it has been a target for cancer research. Bee venom (apitoxin) is a complex toxin containing biologically active components produced by *Apis mellifera*. Its role in selective cytotoxicity in cancer cells has been shown by different studies. However, the discriminating anastatic response of cancerous/non-cancerous cells against bee venom has not been explored before.

Materials and Methods: MCF10A and MDA-MB-231 cells were treated with bee venom for 24h followed by anastatic incubation for up to 72h without bee venom. Trypan blue exclusion method and Annexin-V/PI method were performed by automated cell counter and flow cytometry, respectively.

Results: Bee venom has induced anastasis in only normal breast cells while persistent cell death in triple-negative breast cancer cells[3]. We have also tested the anastasis after one of the well-known chemotherapeutics, cisplatin, and normal cells entered inevitable cell death as well as cancer cells. We revealed anastatic cell profiles by trypan blue assay and showed that there is no significant return from either apoptosis or necrosis of anastatic cells.

Discussion: We propose the term “positive anastasis” which refers to the temporary death of normal cells whereas the irreversible death of cancer cells after the inducement of cytotoxicity (e.g. bee venom). Recently, anastasis has been shown to be a return from different types of cell death than apoptosis. Our results indicate that positive anastasis may be the reversal of non-apoptotic cell death.

Key words: Anastasis, cancer, bee venom, cisplatin, apitherapy.

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References

1.Tang, H. M., Talbot, C. C., Fung, M. C. & Tang, H. L. Molecular signature of anastasis for reversal of apoptosis. *F1000Research* 6, 43 (2017).

2.Tang, H. M. & Tang, H. L. Anastasis: recovery from the brink of cell death. *R. Soc. Open Sci.* 5, (2018).

3.Tetikoglu, S., Akcan, M., Uzuner, U. & Uzuner, S. C. Selective anastasis induction by bee venom in normal cells: a promising strategy for breast cancer therapy with minimal impact on cell viability. *J. Zhejiang Univ. Sci. B* 1–13 (2024) (in press).

Oral Presentation – 23

Effects of Pablociclib in Combination with Ferulic acid on Apoptosis, ER stress and Oxidative stress in breast cancer cell lines

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Introduction and Aim: Breast cancer is the most common cancer among women and a major cause of cancer-related mortality. CDK4/6 inhibitors, such as palbociclib, induce G1 phase arrest by inhibiting RB phosphorylation but face limitations due to resistance and toxicity. Ferulic acid, a plant-derived polyphenol, has shown antioxidant, anti-inflammatory, and anticancer properties. This study aims to explore the synergistic effects of palbociclib and ferulic acid in HR+ and HR- breast cancer cells, while evaluating the potential toxic or protective effects on normal cells.

Materials and Methods: Various techniques were used: MTT assay for cell viability and IC_{50} determination, ELISA kits for TOS, TAS, and MDA levels, JC-1 staining for mitochondrial membrane potential, Western blot for RB and pRB expression, wound healing assay for cell migration, and RT-qPCR for gene expression related to ER stress, oxidative stress, and apoptosis.

Results: At 48 hours, the IC_{50} values for palbociclib and ferulic acid in MCF-7 and MDA-MB-231 cells were 36.23 μM, 84.60 μM, 12.86 μM, and 29.71 μM, respectively, and in MCF-10A cells, 70.25 μM and 55.82 μM. The combined treatment reduced cell viability more than single agents in cancer cells but increased viability in MCF-10A cells. Palbociclib raised oxidative stress in all cell lines, whereas the combination reduced it in MCF-10A cells. Western blot analysis showed reduced pRB levels in all cell lines. Gene expression analysis indicated the combination upregulated ER stress, Oxidative stress and apoptosis markers in cancer cells, but downregulated them in MCF-10A cells, suggesting a protective effect.

Discussion: Our findings provide the first evidence that ferulic acid combined with palbociclib exerts a synergistic effect on both HR+ and HR- breast cancer cells, with potential protective effects on normal cells. This combination may serve as a promising adjuvant or neoadjuvant therapy, highlighting ferulic acid as a valuable natural compound in cancer treatment.

Key words: Breast cancer, Palbociclib, Ferulic acid, Apoptosis

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Oral Presentation – 24

A Chick Chorioallantoic Membrane-Based Experimental Study: Investigating The Angiogenic Potential of *Aronia melanocarpa* and Boron

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Introduction and Aim: Angiogenesis is a vital process in tissue development and regeneration, but also plays a key role in tumor progression. Natural compounds like *Aronia melanocarpa* fruit extract and trace elements such as boron have garnered attention for their modulatory effects on vascular biology. *A. melanocarpa* provides essential nutrients linked to vascular regulation, including vitamins C and K, and potassium. This study aims to investigate the angiogenic potential of Aronia extract and boron—both individually and in combination—using the in ovo chick chorioallantoic membrane (CAM) model.

Materials and Methods: Fertilized chicken eggs were incubated and windowed on embryonic day 5. Treatment groups included *A. melanocarpa*extract (Dr. Aronia) at 10, 100, and 500 µg/mL; Etibor-48 (sodium tetraborate pentahydrate, $Na_8B_8O_{13}\cdot 4H_2O$) at 10, 100, and 500 mM; and selected combination doses (e.g., Bor10+Aronia500, Bor100+Aronia100, Bor500+Aronia10). After 24 hours of exposure, angiogenesis was assessed via image-based quantification of vessel branching points and total vessel area. Fold-change analysis was performed by normalizing the 24-hour data to each group's 0h baseline.

Results: A dose-dependent increase in vessel branching points was observed in the Aronia100 and Aronia500 groups (1.65x and 1.71x, respectively). Boron alone had minimal effect, and some combinations (e.g., Bor10+Aronia500) showed a slight decrease (0.95x), suggesting no additive or synergistic benefit. No significant differences in total vessel area were found across the groups.

Discussion: The findings indicate that *Aronia melanocarpa* extract promotes fine vascular branching without increasing the overall vessel area, suggesting a remodeling rather than proliferative effect. In contrast, boron—whether alone or in combination—did not stimulate angiogenesis and may attenuate Aronia's pro-angiogenic effects when co-administered. These results emphasize the selective angiogenic activity of Aronia and underscore the importance of evaluating interactions in combination therapies.

Key words: Aronia melanocarpa extract, anthocyanin, sodium tetraborate pentahydrate, angiogenesis, CAM assay

Oral Presentation – 25

Bifunctional Cancer Antibody Engineering for Solid Tumors

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Introduction and Aim: Antibody engineering is one of the pioneering field that combines synthetic biology and immunology tools to develop better therapeutic agents. Bispecific antibodies (BiAbs) are among the most utilized applications in this field, and these molecules can be programmed to stimulate multiple pathways for targeted therapies. In this study, we developed and tested an anti-CTLA4/EGFR BiAb to simultaneously generate an immunologic response and exhibit cancer cell-killing activity.

Materials and Methods: In this study, we have combined the binding regions of the CTLA-4 and EGFR antibodies into a single Y- shaped antibody molecule and employed knob-in-hole and cross-MAb strategies to enhance the molecular stability with antibody engineering techniques. The developed BiAb molecules were evaluated for their physical and biological activities.

Results: Our study resulted in developing a unique BiAb molecule capable of binding to T-cells and cancer cells simultaneously. We also described its physicochemical properties and cellular efficiencies.

Discussion: Bispecific antibodies have been proposed for many years, and advances in synthetic biology tools have made their production possible. Currently, 20 BiAbs are in clinical use, having received regulatory approval. This study focused on creating a unique anti-CTLA4/EGFR BiAb molecule, and our findings suggest promising potential for this molecule as a future drug candidate in cancer treatment. Furthermore, the antibody production platform we developed may serve as a template for future antibody development pipelines.

Key words: Bispecific antibody, Antibody engineering

Oral Presentation – 26

Çok Düşük Frekanslı Elektromanyetik Alanın İnsan Akciğer Kanser Hücreleri Üzerindeki Etkilerinin İncelenmesi

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Geleneksel kanser tedavi yöntemleri arasında kemoterapi, radyoterapi, cerrahi ve bunların kombinasyonları yer almaktadır. Bu yöntemler, tedavi sürecinde sağkalımı arttırsa da özellikle tekrarlayan ve metastatik kanser vakalarında sınırlı etkiye sahiptir. Son zamanlarda, geleneksel tedavilere ek olarak, elektromanyetik alan (EMF) terapisi gibi yenilikçi yaklaşımlar kanser hücrelerinin büyümesini ve yayılmasını engelleme potansiyeline sahip, non-invaziv bir tedavi yöntemi olarak dikkat çekmektedir. Çok düşük (3-3000 Hz) ve düşük frekanslı (3-30 kHz) elektromanyetik dalgalar iyonlaştırıcı özelliğe sahip olmadığı için tıp alanında, çeşitli tedavi yöntemlerinde, özellikle kanser tedavilerinde kullanılmaktadır. Bu çalışmada, non-malignant insan akciğer epitel hücreleri (BEAS-2B) ve malignant insan akciğer kanser hücre hattı (A549) kullanılmıştır. Hücreler 4.5 cm çaplı, 15.7 cm uzunluğunda bir selenoid sistem içinde; 20, 40, 60 Hz frekanslarda sinüzoidal dalga formlu ve 1-3 mT aralığında üç farklı manyetik alan şiddetine sahip elektromanyetik alana maruz bırakılarak, EMF' nin hücre canlılığı üzerindeki etkileri incelenmiştir. 4 gün boyunca, günlük 30, 60 ve 90 dakikalık sürelerle EMF' ye maruz bırakılmıştır. Bu işlem, 3 farklı frekans ve 3 farklı manyetik alan şiddeti için tekrarlanarak hücre canlılığının frekansa ve manyetik alan şiddetine bağlı değişimleri incelenmiştir. Maruziyet süresinin sonunda hücre canlılıkları sitotoksisite test yöntemleri ile belirlenmiştir. Sonuç olarak, farklı manyetik alan şiddetinin hücre tipine ve süreye bağlı olarak değişen sitotoksik etki gösterdiği ortaya konmuştur.

Anahtar Kelimeler: Elektromanyetik alan, Akciğer Kanseri, Sitotoksik Etki

Oral Presentation – 27

Development of a Tumor-On-Chip Model to Predict Drug Response in Breast Cancer

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Introduction and Aim: Breast cancer, a highly heterogeneous neoplasm, requires innovative strategies for personalized treatment. Here, we present a novel on-chip approach to evaluate drug response in human breast tumor samples. Previously, we demonstrated this platform's ability to assess drug response and invasion using breast cancer cell lines. In this study, we extend its application to primary breast tissues using core needle biopsy samples.

Materials and Methods: Biopsy samples were obtained from BI-RADS 5-classified breast tumors. A custom-made slicer was used to section tissues into ~400 μm discs. To assess initial viability of the samples for potential exclusion, we used PrestoBlue viability assay. Three tissue slices per trial were incubated at 65 °C for one hour to serve as a negative control representing dead tissue. To account for viability variations arising from biopsy sampling, we established a viability index by comparing mean grey values of samples to negative controls. Samples falling below a predefined threshold were excluded from subsequent drug response experiments.

Results: To optimize tissue viability, we tested various culture media and determined that DMEM-F12 supplemented with EGF, hydrocortisone, cholera toxin, and insulin was optimal. We then assessed tissue viability with and without paclitaxel (1.6–14 μM). Paclitaxel exposure significantly decreased viability within 24 hours, while control samples remained viable for 14 days. For invasion analysis, tissues were stained with a cell tracker and embedded in Matrigel within a tumor-on-chip platform consisting of three interconnected channels. A few cells migrated toward the channel containing 20% FBS as a chemoattractant.

Discussion: Our study demonstrates a cost-effective and less labor-intensive approach for precision oncology. This model enables real-time monitoring of cellular dynamics, including drug responses, offering valuable insights into tumor behavior and potential therapeutic strategies.

Key words: Tumor tissue slice, tumor-on-chip, breast cancer, personalized medicine

Oral Presentation – 28

Deciphering the Molecular Connection Between Ulcerative Colitis and Colorectal Cancer via Integrative Bioinformatic Analysis

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Introduction and Aim: Patients with ulcerative colitis (UC) are at an increased risk of developing ulcerative colitis-associated colorectal cancer (UCAC). However, the molecular mechanisms linking UC and colorectal cancer (CRC) remain unclear. This study aims to uncover shared molecular signatures and identify potential biomarkers and therapeutic targets involved in UCAC development.

Materials and Methods: Microarray datasets for CRC (GSE110224, GSE22598, GSE21815) and UC (GSE83687, GSE92415, GSE87473) were obtained from the Gene Expression Omnibus (GEO). Differentially expressed genes (DEGs) were identified by comparing tumor or UC samples with controls. Overlapping DEGs were determined, and upregulated genes were prioritized due to their therapeutic relevance. Cancer hallmark gene sets analysis using GSEA was performed for both CRC and UC. Shared pathways and common genes were identified to uncover molecular connections. Candidate gene expression was validated in independent datasets, and progression patterns from control to UC to UCAC were assessed. Prognostic value was evaluated through survival and regression analyses.

Results: A total of 1147 and 1014 DEGs were identified in CRC and UC, respectively. Nineteen common cancer hallmark pathways, including Epithelial-Mesenchymal Transition (EMT), Inflammatory Response, TNF-α Signaling via NF-κB, and Hypoxia, were enriched in both diseases. Twenty-four EMT-related genes were shared, with 23 validated in external datasets. Among the 13 key genes associated with UCAC—INHBA, CXCL1, COL12A1, MMP1, MMP3, SPP1, TIMP1, TGM2, CTHRC1, FAP, CALU, CD44, and TGFBI—four genes (CALU, TGFBI, COL12A1, and MMP1) showed a consistent increase in expression from control to UC to UCAC. Importantly, this study is the first to identify CALU, TGFBI, and COL12A1 as UCAC-related genes.

Discussion: This study reveals shared molecular alterations between UC and CRC, highlighting CALU, TGFBI, and COL12A1 as novel candidate biomarkers for UCAC. These findings offer potential for improving early detection and targeted strategies in UC patients at elevated risk of CRC.

Key words: Ulcerative colitis, colorectal cancer, ulcerative colitis-associated colorectal cancer, biomarker, therapeutic target, bioinformatic analysis

Oral Presentation – 29

Effects of Sanguinarine and Thionicotinamide Molecules on Temozolomide-Resistant Cells in Glioblastoma

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Introduction and aim: Glioblastoma is the most common malignant brain tumor with a high mortality rate. Despite surgery followed by radiotherapy and TMZ chemotherapy, tumors often relapse within 15 months, progressing to high-grade glioma. This leads to genomic instability and increased ROS levels, which disrupt cell homeostasis and induce cytotoxicity. In glioblastoma, NADPH metabolism, which regulates ROS neutralization, differs between healthy and cancerous tissues. To exploit this difference, it is aimed to increase ROS formation by targeting NADPH metabolism with combined applications of Sanguinarine (SNG) and Thionicotinamide (TIO) molecules.

Materials and Methods: TMZ-resistant U87-MG and LN-18, TMZ-sensitive LN229 were used as cancer cells, and HUVEC cell line was used as healthy cells. SNG and TIO molecules were applied to the cells at appropriate concentrations. Cell viability, intracellular ROS level, NADPH levels and apoptosis assays were performed, and gene expression levels of genes related to NADPH metabolism were investigated.

Results: While no molecule affects cell viability in healthy cells, it was observed that especially combined treatments decreased cell viability by 60-70%. Furthermore, the increase in ROS was observed to be more pronounced in TMZ-resistant cells compared to TMZ-sensitive cells. While SNG molecule increased expression of NOX5 gene by approximately 2-fold, TIO decreased NADK2 gene expressions. In resistant cells, the combined application of the molecules resulted in a further depletion of the intracellular NADPH pools.

Discussion: In TMZ-resistant and sensitive glioblastomas, SNG and TIO molecules increased ROS formation by re-regulating NADPH metabolism and rapidly caused cell death. Combined application of these two molecules can replace TMZ, which is widely used in glioblastoma treatment.

Key words: Sanguinarin, Thionicotinamide, Glioblastoma, Resistance, ROS, NADPH

Oral Presentation – 30

Imipramine Suppresses Cellular Survival by Regulating Ferroptosis via SOX10/Gpx4/ACSL4 Signalling and Iron Metabolism in Colerectal Cancer

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Introduction and Aim: In the last decade, second and third-generation antidepressants with fewer side effects have been widely preferred in oncology. However, since sufficient evidence has not yet been obtained in humans, it is unclear how the results will be interpreted as a true cancer treatment. Overall, our studies suggest that antidepressants could be a promising approach in cancer treatment. Colorectal cancer is one of the most common types of cancer worldwide, accounting for approximately 7% of all cancer cases. In this study, we aimed to investigate the effects of imipramine, a tricyclic antidepressant, on colorectal cancer.

Materials and methods: First, the cytotoxic effects of imipramin on Caco-2 cells were assessed using MTT assays. Subsequently, SOX10, GPX4, ACSL4, GSH, MDA, total ROS, Fe^{2+}, and TFR levels were analysed using ELISA, and RT-PCR techniques.

Results: According to the cell viability analysis, the IC_{50} and low dose value for imipraminewas determined to be 60 and 15 μg/mL in Caco-2 cells. In cells treated with 15, 60, and 90 μg/mL concentrations of imipramine for 24 hours. RT-PCR analyses revealed that SOX10 expression was significantly higher in Caco-2 cells. Imipramine also reduced GSH, GPX4, and SOX10 levels in cells, while inducing an increase in MDA, total ROS, ACSL4, Fe^{2+} and TFR levels.

Discussion: İmipramine has been shown to have Fascin1-dependent anti-invasive and anti-metastatic effects in colorectal cancer cells. One of the studies of our group on antidepressants in cancer is that imipramine has shown its effect on ferroptosis in colorectal cancer.

Key words: Imipramin, Caco-2, ferroptosis, Cancer, Oxidative stress

Oral Presentation – 31

Evaluation of The Effects of miR-30d-3p on Proliferation, Migration, and Cell Cycle in A549 Cells Under Normoxic and Hypoxic Conditions

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Introduction and Aim: Hypoxia promotes genomic instability, tumor aggressiveness, and resistance in lung cancer. The tumor suppressor, miR-30d-3p, is upregulated under hypoxic conditions, suggesting a functional role in tumor progression. This study examines the effects of miR-30d-3p on proliferation, cell cycle, and migration in A549 cells cultured under normoxic or hypoxic conditions.

Materials and Methods: The effects of miR-30d-3p on cell proliferation and migration were evaluated using RTCA, and the cell cycle was assessed by flow cytometry. The expression levels of hsa-miR-30d-3p, JMY, p53, cell cycle-related genes, and proliferation-related genes in A549 cells under normoxic and hypoxic conditions were analyzed by RT-PCR.

Results: The hypoxia conditions increased the expression levels of hsa-miR-30d-3p (6.1 fold) in A549. In addition, the cells transfected with miR-30d-3p inhibitor reduced cell proliferation to 73.1%, 56.9%, and 65.7% at 24, 48, and 72h, respectively. The number of A549 cells increased in the G1 phase (62%) in the presence of miR-30d-3p mimic compared with the negative mimic control (49.2%) under normoxic conditions. In the transfection of cells with miR-30d-3p inhibitor for 72 h under hypoxic conditions, the cell number was slightly increased in the Sub-G1 and G1 phases. Under normoxic conditions, overexpression of miR-30d-3p resulted in a reduction in A549 cell migration by up to 48.4%. Overexpression or inhibition of miR-30d-3p did not show any effects on the A549 cell migration rate under hypoxia conditions, however, the A549 cell migration was reduced in the presence of hsa-miR-30d-3p mimic under normoxia conditions. mRNA expression levels varied in response to hsa-miR-30d-3p mimic and inhibitor treatments.

Discussion: miR-30d-3p may serve as a therapeutic target for lung cancer. Overexpression of miR-30d-3p in A549 cells under normoxia reduces migration and induces G1 arrest. Under hypoxia, the suppression of physiological miR-30d-3p expression led to reduced proliferation and modest cell cycle arrest.

Oral Presentation – 32

The stemness effect of piRNAs on ovarian cancer stem cells via *in vitro* and *in silico* analysis

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Introduction and Aim: Ovarian cancer (OC) is the fifth most lethal cancer among women and mostly develops chemoresistance, metastasis and the recurrence. The cancer stem cells (CSC) are the significant factors on these mechanisms. One of the epigenetic regulators of CSCs is small piwi-interacting RNAs (piRNAs) which can be used as targets due to their effects on the formation of CSCs. We aimed to investigate the stemness effects of the piRNAs (piR-823, piR-36712, and piR-020326) in OC.

Materials and Methods: The piRNAs' stemness effects were evaluated on OVSAHO by siRNA inhibitor (i) and mimic (m) transfections, and by analyzing the expression levels of stemness genes (*ALDH1A1*, *ALDH1A2*, *ALDH1A3*, *SOX2*, *CD133* and *NANOG*) in both 2D adherent and 3D spheroid cultures using qRT-PCR. The piRNA and stemness genes expression levels were calculated using the $2^{-\Delta\Delta\Delta Ct}$ method in GraphPad Prism (v9.2.0). To support the experimental findings, transcriptomic data from TCGA (Recurrent OC, Primary OC) and GEO (Ovarian CSC) databases were analyzed. FPKM values were imported into R (v4.4.1) and min-max normalization and log2 transformation were applied to improve comparability. Differential expression of significant genes was analyzed using DESeq2 to the identification of potential biomarkers and key genes regulating stem cell properties.

Results: PiR-823 (i) and piR-020326 (i) acted as negative regulators on CSCs by stemness genes inhibition, while piR-36712 increased the expression of stemness genes, *ALDH1A1* and *CD133*. Bioinformatic analyses revealed increased expression of *NANOG*, *SOX2*, *CD133*, *ALDH1A1*, and *ALDH1A3* in recurrent tumors. These results support the potential targets of these piRNAs that may influence CSC characteristics in OC.

Discussion: While the inhibition of piR-823 and piR-20326 plays a suppressive role in CSC development, piR-36712 supports the maintenance of stemness characteristics. *In vitro* and *in silico* analyses were showed a potential effect of piRNAs on OCSC by stemness gene regulations.

Key words: ovarian cancer, cancer stem cells, piRNAs, in-silico analysis

Oral Presentation – 33

Akciğer Skuamöz Hücre Karsinomunun Tani Ve Prognozu İçin Potansiyel Mirna Biyomarker Paneli

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Giriş ve Amaç: Akciğer kanseri dünyada kanserle ilişkili ölümlerin çoğundan sorumludur. Küçük hücreli ve daha sık rastlanılan küçük hücreli dışı akciğer kanserleri şeklinde iki ana akciğer kanseri türü vardır. Akciğer adenokarsinomundan sonra, akciğer skuamöz hücreli karsinomu, küçük hücreli dışı akciğer kanser türleri arasında en yaygın görülen alt türlerden biridir. Akciğer skuamöz hücreli karsinom genellikle spesifik semptomlar göstermediğinden tanısı ilerleyen safhalarda yapılır ve maalesef hastalığın sağ kalım oranı oldukça düşüktür. Bunun yanı sıra, akciğer skuamöz hücreli karsinomunun tanı veya tedavisini iyileştirmek için yapılan araştırmalar diğer akciğer kanseri alt tiplerine kıyasla oldukça geri plandadır. Bu bilgiler doğrultusunda, skuamöz hücreli karsinomu için daha iyi tanı ve prognoz yaklaşımları sağlayabilecek yeni yöntemlere ihtiyaç olduğu açıktır. Klinikte miRNA biyomoleküllerinin avantajları ve biyomarker panellerinin (biyomarker kombinasyonlarının) potansiyeli göz önüne alınarak, bu çalışmada akciğer skuamöz hücreli karsinomunun tanı ve prognozunda kullanılabilecek miRNA biyomarker panellerini bulmak için biyoinformatik temelli bir yaklaşım uygulandı.

Materyal ve Metot: Bu çalışmada, kanser ve normal biyolojik örnekler arasında farklı şekilde ifade gösteren miRNA'lar (DE-miR), birden fazla miRNA ekspresyon verisi kullanılarak bulundu. Kullanılan farklı ekspresyon verilerinde ortak çıkan ve ekstraselüler olarak bulunan DE-miR'ler kullanılarak en iyi tanısal miRNA kombinasyonlarını belirlemek için CombiROC algoritması uygulandı ve işlem karakteristik (ROC) eğrisi analizi yapıldı. İstatiksel olarak tanı kapasitesi yüksek bulunan DE-miRNA kombinasyonlarının prognostik kapasitelerini de değerlendirmek için Kaplan-Meier yöntemi kullanıldı ve sağkalım analizleri gerçekleştirildi.

Sonuç: Akciğer skuamöz hücreli karsinomu için 5 DE-miR'den oluşan istatiksel olarak yüksek tanı ve prognoz kapasitesine sahip özgün bir biyomarker paneli bulundu.

Tartışma: Bulunan bu panel, skuamöz hücreli karsinomunun tanısında, prognozunda ve/veya önlenmesindeki potansiyeli göz önünde bulundurularak ileriki deneysel ve klinik çalışmalara yol gösterici olacaktır.

Oral Presentation – 34

Rac1 Signaling Modulates Autophagic Balance in Mammary Epithelial Cells: A Mechanism Linked to Postlactational Involution and Cancer

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Introduction and Aim: The mammary gland is a unique organ that undergoes dynamic tissue remodeling to support its development and function. During postlactational involution, autophagy is upregulated to maintain cellular homeostasis. However, the remodeling of the mammary microenvironment during involution creates an inflammatory milieu that can promote metastasis in pregnancy-associated breast cancer. This study aims to elucidate the role of Rac1 signaling in the regulation of autophagy in mammary epithelial cells. Rac1 is frequently upregulated in cancers, including breast cancer, and is known to regulate cytoskeletal dynamics, cell survival, proliferation, and invasion.

Materials and Methods: To investigate the molecular mechanisms underlying Rac1-mediated regulation of autophagy, autophagy was induced by Oncostatin M (OSM) in mammary epithelial cells with genetically or pharmacologically altered Rac1 activity. Autophagic responses were assessed via immunoblotting, immunofluorescence and qPCR.

Results: OSM-treated Rac1-overexpressing cells showed increased mRNA expression of autophagy-related genes, while LC3 degradation was reduced—suggesting dysregulated or unbalanced autophagy. p62 accumulation was confirmed through immunoblotting and puncta analysis. Interestingly, phosphorylated Stat3 levels were elevated in Rac1-depleted cells, whereas LC3 lipidation remained unchanged.

Discussion: Rac1-mediated modulation of autophagy in mammary epithelial cells may contribute to the pro-tumorigenic microenvironment observed during postlactational involution, potentially facilitating breast cancer progression. In addition, the accumulation of p62 likely reflects impaired lysosomal degradation or proteasomal dysfunction rather than a block in LC3 lipidation. Rac1 may also be involved in modulating the ubiquitin–proteasome system (UPS), a possibility that warrants further investigation.

Key words: Autophagy, Rac1 signaling, Mammary gland remodeling, Breast cancer

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Oral Presentation – 35

Targeting p53-negative cancer cells for killing by novel oncolytic Adenoviruses whose replication is driven by a p53-regulated promoter

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Introduction and Aim: Mutation in p53 leads to loss of its transcription factor function, resulting in uncontrolled cell division and carcinogenesis. Approximately 50% of cancers have point mutations or deletions in the p53 gene. While normal (wt) p53 directly activates the transcription of hundreds of genes, there is a group of genes whose transcription is repressed by wtp53. We have used promoter elements from one such wtp53-repressed gene to drive gene-based cancer therapies. Oncolytic Adenoviruses (Ads) offer a promising approach to cancer therapy. Here we describe proof-of-concept experiments using Ads that contain wtp53- repressible promoters to discover whether these modifed Ads can selectively kill p53-negative cancer cells with reduced cytotoxic effects on p53-positive or non-cancer cells.

Materials and Methods: Two Ads were constructed in which the viral E1A promoter was replaced by a segment (termed "short" or " long") of a p53-repressible promoter. These recombinant viruses were generated from a chimeric Ad type 5 containing the fibre of Ad type 35 (Ad5/F35). Selective replication and cell-killing by these Ads were determined on colon, pancreatic and lung cancer cell lines.

Results: In two- and three-dimensional cell systems, Ad5/F35-long showed approximately two-fold increased replication and cell-killing ability in p53-negative colon cancer cells compared to p53-positive and non-cancer cells. Ad5/F35-long also showed increased replication and cell-killing ability in p53-negative pancreatic and lung cancer cells compared to p53-positive cancer cells in two-dimensional cell systems. Ad5/F35-short also showed significant replication and cell killing in colon, pancreatic and lung cancer cell lines.

Discussion: These oncolytic Ads are able to infect, replicate and kill p53-negative cancer cells. The Ad containing the longer promoter might be more selective for p53-negative cells than the Ad with the shorter promoter. Overall, the Ad containing the longer promoter fragment may form the basis of a novel cancer therapy that selectively targets p53-negative cancer cells.

Key words: P53-negative cancer, p53-repressed genes, Oncolytic Adenoviruses

Oral Presentation – 36

Comparative Analysis of Pulmonary Vein Extracellular Vesicle-Derived Whole Transcriptome Signature in Lung Adenocarcinoma using RNA-Sequencing

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Introduction and Aim: Extracellular vesicles (EVs), present in almost all body fluids, serve as pivotal mediators of intercellular communication by transporting diverse biomolecules—such as nucleic acids [including DNA, mRNA, microRNA (miRNA), and long non-coding RNA (lncRNA)], proteins, and lipids— intercellular communication, thereby facilitating molecular exchange and signaling. Tumor-derived EVs modulate the tumor microenvironment in recipient cells, affecting cancer progression through metastasis, tumor growth, and invasion. Pulmonary blood contained higher EV levels than peripheral blood, indicating pulmonary EV potential as stage-reflective diagnostic and prognostic markers in lung cancer. This study examined EV cargo in pulmonary versus peripheral veins of non-small cell lung cancer (NSCLC) patients across early tumor stages and profiled their transcriptome cargo to identify biomarkers associated with progression and aggressiveness.

Materials and Methods: Pulmonary vein serum samples were collected perioperatively from six NSCLC patients (stage 0 and stage 1, n=3 for each group). EVs were isolated and characterized using Western blotting and nanoparticle tracking analysis (NTA), followed by RNA extraction. cDNA libraries were constructed for RNA sequencing, and subsequent bioinformatic analyses were performed to evaluate expression profiles. Differentially expressed mRNAs, miRNAs and lncRNAs were further investigated through target prediction and pathway enrichment analyses. Additionally, their expression patterns were compared with publicly available datasets from the Cancer Genome Atlas (TCGA) and Genotype-Tissue Expression (GTEx).

Results: NTA showed ~1.5-fold higher EV concentration in pulmonary versus peripheral venous samples. Pulmonary EV-derived transcriptome signatures showed between N0 and N1 stage patients, with 77 mRNAs, 10 miRNAs and 18 lncRNAs common to both stages. A total of 53 mRNAs, 6 miRNAs

and 10 lncRNAs were dysregulated in N0, while 46 mRNAs, 7 miRNAs and 8 lncRNAs showed dysregulation in N1 ($P<0.05$, logFC ≥ 2 or ≤ -2).

Conclusion: As the pulmonary vein is anatomically closest to the primary tumor site, it is likely that the RNA content identified in these EVs predominantly reflects the molecular characteristics of the tumor tissue. These findings support the potential utility of pulmonary vein-derived EVs as a rich source of tumor-specific transcriptomic-based biomarkers for NSCLC detection and monitoring.

Key words: lung cancer, extracellular vesicles, liquid biopsy, transcriptomics.

Oral Presentation – 37

Epigenetic Changes in Tumor Suppressor Genes in Triple Negative Breast Cancer Patients

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Introduction and Aim: Epigenetics refers to heritable changes in gene expression that do not result in changes in the DNA sequence. DNA methylation is one of the important mechanisms that cause loss of function in tumor suppressor genes. Triple Negative Breast Cancer (TNBC) is a type of invasive breast cancer that is deficient in estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). SFRP1 gene methylation may affect cancer cell proliferation and metastasis. Our aim is to reveal the methylation patterns of SFRP1 in patients with TNBC, which is aggressive and associated with poor prognosis, and to examine its relationship with the disease.

Materials and Methods: Paraffinized breast tissue samples were taken from 86 TNBC patients in this retrospective study. DNA was isolated from tissue and converted to bisulfite form for MSP-PCR to evaluate methylation status of SFRP1 gene. Statistical studies were carried out on the data obtained as a result of the study.

Results and Conclusion: As a result of the study, it was determined that the SFRP1 gene was methylated in 83.7% of the patients. Additionally, a moderately positivity of SFRP1 methylation and statistically significant correlation was found between Ki-67 and grade ($p<0.01$). In conclusion, the methylation of the SFRP1 gene in TNBC patients suggested that epigenetic changes on tumor supressor genes are effective in the development and progression of cancer.

Key words: Epigenetic, Methylation, SFRP1, TNBC, Tumor suppressor gene

Oral Presentation – 38

Restoring Sensitivity to Midostaurin in FLT3-ITD AML Cells Through Resveratrol Co-Treatment

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Introduction and Aim: FMS-like tyrosine kinase 3-internal tandem duplication (FLT3-ITD) mutations are present in 20-25% of acute myeloid leukemia (AML) patients and often associated with poor prognosis, reduced response, and a higher risk of relapse. Although there are clinically approved FLT3 inhibitors such as midostaurin, development of acquired resistance to these inhibitors remains a significant challenge. Resveratrol, a natural polyphenol with anti-cancer properties, has emerged as a potential therapeutic agent against drug resistant cancer. In this study, we investigated the effects of resveratrol in combination with midostaurin, aiming to enhance the sensitivity of midostaurin-resistant FLT3-ITD AML cells.

Materials and Methods: To evaluate the effects of resveratrol on acquired midostaurin resistance, midostauin-resistant MV4-11 and MOLM-13 cell lines were generated. The antiproliferative effects of resveratrol in combination with midostaurin were investigated using MTT assay. Combination indexes were calculated to determine if the combination of resveratrol with midostaurin was synergistic. Cell cycle arrest was analyzed by PI staining. Late and early apoptosis was detected by annexin V/PI double staining by flow cytometry. Apoptotic proteins including cleavages of caspase-3 and PARP, Bax and Bcl-2 levels were determined by western blotting. FLT3/STAT5A axis was evaluated through the protein expression levels of p-FLT3 and p-STAT5A.

Results: The combination of resveratrol and midostaurin significantly inhibited cell proliferation and demonstrated additive or synergistic effect, as determined by the Chou-Talalay Combination Index. The combination treatment induced cell cycle arrest and promoted apoptosis. Mechanistically, the combination treatment increased the cleaveges of caspase-3 and PARP, accompanied by elevated Bax/Bcl-2 ratios. Combination treatment also reduced the expression levels of p-FLT3/FLT3 and p-STAT5A/STAT5A.

Discussion: Resveratrol enhances the sensitivity of midostaurin-resistant FLT3-ITD AML cells by inhibiting proliferation and inducing apoptosis through downregulation of FLT3/STAT5A axis. Thus, combination of resveratrol with midostaurin might be a potential therapeutic strategy to overcome midostaurin resistance in FLT3-ITD AML.

Key words: FLT3-ITD AML, Resistance, Resveratrol, Midostaurin

Oral Presentation – 39

Examining the apoptotic effects of novel isoxazole-quinoline derivatives on different cancer cell lines

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Introduction and Aim: Cancer is a disease that occurs with uncontrolled cell proliferation and is the second leading cause of death in the world. Isoxazole and quinoline represent an important class of heterocycles that are widely used in synthesis, possess diverse biological activities, and serve as unique pharmacophores present in many therapeutic agents. Aim of this study is to investigate the apoptotic effects of new hybrid molecules combining 8-aminoquinoline and isoxazole rings on various cancer cells, which may be promising anticancer agents.

Materials and Methods: After the cell viability analysis was performed on the synthesized fourteen molecules in four different cell lines by Cell Titer-Glo, the further biochemical experiments continued with the most potent two novel molecules, C10 and C14. To investigate whether the molecules trigger apoptosis in A549 and SKOV3 cells, the level of PARP protein was examined by western blot method and used Annexin V/PI staining in flow cytometry to detect the apoptosis/necrosis ratio in SKOV3 cells treated with C10. Besides migration ratio was measured by scratch assay.

Results: It was observed that our novel molecules 10 and 14 at the concentrations of 20 μM for 48 hours markedly reduced the level of PARP compared to control. Also, Annexin V/PI staining showed that the apoptosis ratio was significantly increased with C10-treated SKOV3 cells for 48 hours. In addition, scratch assay studies found that SKOV3 cells treated with C10 for 48 hours considerably inhibited cell migration.

Discussion: These studies have shown that C10 induces apoptosis in SKOV3 at low drug concentrations with no toxic effect on healthy cells, indicating that it could be a promising therapeutic target. It is recommended to investigate this compound the mechanisms of action in cancer signaling pathways with further biochemical analyses.

Key words: Anticancer activity; Isoxazole; Quinoline; Novel heterocyclic isoxazole-quinoline derivatives

Oral Presentation – 40

Investigation of the Effect of Exportin-1 Gene Inhibition with Selinexor on Meningioma

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Introduction and Aim: Brain metastases, meningiomas, and glioblastomas are among the most common brain tumors. Meningiomas lack a standard therapeutic agent, with treatment depending on tumor size, location, and growth rate. Management typically involves monitoring or surgery, with radiotherapy for inoperable or recurrent cases. Therefore, new treatment strategies are needed. XPO1, a nuclear export protein, regulates the transport of numerous tumor suppressors, proteins and RNA. Its dysregulation contributes to cancer progression and drug resistance. Investigating XPO1's role in meningiomas and the potential of its inhibition could aid in developing new therapies.

Materials and Methods: Meningioma cell line IOMM-Lee was used as a cancer cell model. The XPO1 inhibitor Selinexor was administered in combination with TMZ in cell lines. The effects of these combinations on cell viability were assessed. Mechanisms of effective combinations elucidated by examining apoptosis, cell cycle analyses, colony formation and changes in the expression levels of related genes.

Results: It was observed that the inhibition of XPO1 with Selinexor, when used in combination therapy, significantly reduced cell viability in meningioma cell lines compared to each drug administered alone. Additionally, it was found that TMZ alone halts the cell cycle at the S phase in meningiomas, whereas combining it with Selinexor shifts the cell cycle arrest to the G1/G0 phase. Lastly it was found that combination treatment suppressed DNA damage repair genes.

Discussion: The inhibition of XPO1 by Selinexor appears to play a crucial role in brain cancer treatment by enhancing the efficacy of chemotherapy agents. This inhibition may strengthen the therapeutic impact of these drugs, making treatment more effective. Additionally, the combination of Selinexor and TMZ could significantly reduce the likelihood of tumor recurrence, suggesting a synergistic effect that warrants further investigation in clinical settings.

Key words: Meningioma, XPO1, Selinexor

Oral Presentation – 41

Üçlü Negatif Meme Kanserlerinde Flavopiridol, Sinnamik Asit Ve Kombinasyonlarının Terapötik Ajan Olarak İn Vitro Araştırılması

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Giriş/Amaç: Meme kanseri yüksek ölüm ve nüks etme oranı ile dünya da kadınlar arasında en yaygın kanser tipidir. Meme kanser alt tiplerinden üçlü reseptör negatif meme kanseri üç reseptöründe olmadığı en agresif tiptir. Üçlü reseptör meme kanseri kemoterapötiklere karşı dirençli ve kolaylıkla hedeflenemediği için yan etkisi daha az doğal içerikli yeni tedaviler geliştirilmek zorundadır. Bu çalışmada Dysoxylum binectariferum'dan elde edilen siklin bağımlı kinaz inhibitörü olan yarı sentetik flavopiridol ve doğal aromatik karboksilik asit olarak bilinen sinnamik asit ve bu iki bileşiğin kombin uygulaması kullanılarak yeni kemoterapötik geliştirmek amaçlanmıştır.

Materyal/Metot: Flavopiridol, sinnamik asit ve kombinasyonlarının üçlü negatif meme kanseri olan MDA-MB-231, BT-549 ve BT-20 hücrelerinde canlılık/proliferasyon, klon oluşumu ve yara iyileşmesi incelenmiştir. Canlılık/proliferasyon için MTS analizi, klon oluşumu için klonojenik analiz ve yara iyileşmesi için migrasyon deneyleri yapılmıştır.

Sonuçlar: Yapılan deneyler sonucunda istatistiksel analizler yapılmış olup flavopiridol ve sinnamik asitin kombin uygulamasının sadece flavopiridol ve sadece sinnamik asit bileşiklerinin uygulamasından daha etkin olduğu gösterilmiştir.

Tartışma: Sonuç olarak flavopiridol ve sinnamik asit kombin tedavisi, üçlü negatif meme kanserlerinde umut verici kemoterapötik olarak sunulmuştur.

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Anahtar Kelimeler: Flavopiridol, sinnamik asit, üçlü negatif meme kanseri, terapötik ajan.

Oral Presentation – 42

Vitamin D Modulates Proliferation and Energy Metabolism Through Perilipin2 Pathway in MCF-7 Breast Cancer Cells

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Introduction and Aim: Doxorubicin, one of the chemotherapeutic agents used in the treatment of breast cancer, has strong anticancer properties, but its side effects and resistance development create limitations in clinical applications. Vitamin D attracts attention with its potential antitumor properties. In this study, the effects of separate and combined application of doxorubicin and vitamin D were investigated in MCF-7 breast cancer cell line.

Materials and Methods: The proliferative properties of doxorubicin and vitamin D applied at log concentrations were evaluated based on cytotoxic effects. MCF-7 cells were incubated for 24 and 48 hours.

Results: Doxorubicin application dramatically suppressed cell proliferation approximately X2 fold, within combination 1nM of vitamin D added to the application, reduced proliferation in a controlled manner and reprogrammed cellular metabolism. Also, Vitamin D application increased perilipin expression, promoted the formation and stabilization of lipid droplets, while doxorubicin accelerated lipolysis processes by causing a decrease in perilipin levels. These metabolic changes were associated with the regulation of cellular energy homeostasis via carbohydrate metabolic pathways.

Discussion: It is thought that combined treatment with doxorubicin and vitamin D provides a metabolic reprogramming that supports the transition from glycolysis to oxidative phosphorylation in MCF-7 cells, which increases the efficiency of energy production in cells and strengthens anti-carcinogenic effects. These findings support the potential of vitamin D as an adjuvant agent for chemotherapy, apart from doxorubicin and derivative agents used as routine treatment, and are promising for new treatment approaches.

Key words: Doxorubicin, vitamin D, MCF-7, PLIN2, energy metabolism

Oral Presentation – 43

Anticancer Activities of Dopamine and Histamine Ligands of Usnic Acid

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Introduction and Aim: Usnic acid, dopamine and histamine appear to be potential therapeutics for cancer cells. Dopamine is a neurotransmitter, and histamine acts as both a hormone and a neurotransmitter, depending on its location. In this study, the anticancer activities of dopamine, histamine and ligands of usnic acid in different cancer cell lines (PC-3, HepG2 and MCF-7) were investigated.

Materials and Methods: Cell viability test (MTT), was performed first, and then the clonogenicity test (colony assay) was performed to determine the effects of those with cytotoxic effects on the ability to form colonies in different (treatment and control) cell lines. Finally, OSI (oxidative stress index) was calculated to reveal the relationship between the cytotoxic effect in cells and oxidative stress.

Results and Conclusion: Usnic acid ligands have strong cytotoxic effect on cancer cells and this effect caused by oxidative stress leading to apoptosis. As concluded, usnic acid dopamine and histamine ligands are bright molecules for cancer studies.

Key words: Usnic acid, Dopamine, Histamine, Anticancer, Lichen.

Oral Presentation – 44

Investigation of the Synergistic Effects of Resveratrol and Cisplatin on Lung Cancer and Cisplatin-Resistant Cell Lines

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Introduction and Aim: Non-small cell lung cancer (NSCLC) is the most common subtype, and chemotherapy resistance remains a major challenge. Cisplatin is widely used, while resveratrol, a natural polyphenol, may enhance chemotherapy efficacy and reduce side effects. This study explores the effects of resveratrol and cisplatin, both alone and in combination, on A549(lung cancer) and A549/CDDP(cisplatin-resistant) cell lines.

Materials and Methods: The cytotoxic, apoptotic and autophagic effects of resveratrol and cisplatin were assessed via MTT assay, Annexin V/PI flow cytometry, Autophagic vesicles visualized by fluorescent labeling.

Results: After 48 hours of incubation, the IC_{50} doses of cisplatin and resveratrol were 24.91µM and 122.5µM in A549, 51.52µM and 100µM in A549/CDDP, and 21.2µM and 154.7µM in BEAS-2B (healthy lung) cells. Resveratrol showed a stronger effect on resistant cell lines than on A549 cells, with a lower effect on healthy BEAS-2B cells. Combination ratios of 10%, 20%, 30%, 40%, 50%, 75% and 100% of the IC_{50} doses of cisplatin and resveratrol were prepared and their combination indices were calculated. The results indicated an antagonistic effect at 10% and a synergistic effect at 40% and 50%, leading to the selection of these ratios for further evaluation of their apoptotic effects. In A549/CDDP cells, apoptosis rates were 16.79%(cisplatin), 16.52%(resveratrol), and 5.15%, 11.53%, and 21.1% for 10%, 40%, and 50% combinations, respectively. In A549 cells, apoptosis rates were 20.44%(cisplatin), 15.29%(resveratrol), and 10.77%, 14.8%, and 17.84% for the same combinations. Apoptosis was higher at the synergistic combination ratios of 40% and 50%. While autophagic vesicle signal intensity decreased in the A549 cell line, no significant difference in signal intensity was observed in the A549/CDDP cell line.

Discussion: In conclusion, resveratrol and cisplatin showed a synergistic apoptotic effect at 40% and 50% doses, with selective cytotoxicity in resistant cells. Autophagic activity decreased in A549 cells but remained unchanged in A549/CDDP cells.

Oral Presentation – 45

Liquidambar orientalis induces apoptosis in the MDA-MB-231 breast cancer cell line through the upregulation of P53 expression

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Characterized by its high aggressiveness, poor prognosis, frequent recurrence, and low survival rates, triple-negative breast cancer (TNBC) often displays promoter hypermethylation of epigenetic biomarker genes within the tumors. The challenges associated with current cancer therapies, intensive drug use, and their adverse effects on patients' quality of life have encouraged the investigation of herbal products as alternative therapeutic approaches. This study aims to investigate for the first time the effects of the plant *Liquidambar orientalis*, known for its anticancer properties, on apoptosis and DNA methylation in MDA-MB-231, a TNBC cell line.

The MTT assay was used to determine the doses of *Liquidambar orientalis*. Gene methylation status was analyzed using Methylation-Specific PCR (MSP). Following protein isolation from both treated and untreated cells, the expression levels of proteins were determined using Western blotting. Western blot band intensities were quantified with the ImageJ program.

According to the MTT assay results, the half-maximal inhibitory concentration (IC_{50}) of *Liquidambar orientalis* on the MDA-MB-231 cell line was determined to be 250 µg/ml. MSP analysis indicated that treatment with *Liquidambar orientalis* was associated with the unmethylation of CASPASE-9, CASPASE-3, and P53 genes. Furthermore, Western blot results demonstrated that *Liquidambar orientalis* treatment decreased the protein expression levels of DNMT1, CASPASE-9, and CASPASE-3, while it increased P53 protein expression levels.

These results indicate that Liquidambar orientalis could potentially induce apoptosis through the upregulation of P53 expression and downregulation of DNMT1 expression. These results support the anticancer potential of *Liquidambar orientalis* and highlight the importance of herbal approaches in breast cancer treatment.

Key words: Liquidambar orientalis, MDA-MB-231, Apoptosis, DNA methylation.

Oral Presentation – 46

İndol Türevi NN-Dimetil-4-(1-Metil-3(4-Nitrofenil)-1h İndol-2-İl) Anilin Bileşiğinin Sentezi, Karakterizasyonu ve Akciğer Kanseri Hücrelerinde Antikanser Etkilerinin Araştırılması

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Giriş ve Amaç: Küçük hücreli dışı akciğer kanseri mortalitesinin yüksek olması dünyada ve ülkemizde en yüksek seviyede sağlık sorunu oluşturmaktadır. Akciğer kanseri ve tüm diğer kanser türlerinin tedavi aşamalarında kullanılan standart kemoterapi ilaçları ağır yan etkilere neden olmakla birlikte etkin tedavi sağlayamamaları ve direnç gelişimi sorunu nedeniyle akciğer kanserinin tedavisinde yeni, etkili ve güvenli alternatif terapi ajanlarına ihtiyaç duyulmaktadır. Kanser araştırmalarında yeni sentezlenen moleküllerin antikanser etkinliklerinin araştırılmasına son yıllarda çokça yer verilmektedir. İndol türevi bileşiklerin farklı kanser hücrelerinde birçok biyolojik etkileri araştırılmış olup bu çalışmada sentezlenen N,N-dimetil-4-(1-metil-3(4-nitrofenil)-1H indol-2-il) anilin bileşiğinin antikanser etkinliklerini araştıran bir çalışma literatürde henüz yer almamaktadır. Bu çalışmada, yeni sentezlenen olan indol bileşiğinin sentezi, karakterizasyonu, tetiklediği ölüm mekanizmaları küçük hücreli dışı akciğer kanseri hücrelerinde normal akciğer fibroblast hücreleri ile karşılaştırmalı olarak araştırılmıştır.
Materyal ve Metodlar: Antikanser etkinliklerin araştırılmasında MTT tekniği ile sitotoksik etkiler, geçirimli elektron mikroskopi (TEM) kullanılarak ise ince yapı değişiklikleri ve poapoptotik etkiler araştırılmıştır.
Bulgular: Küçük hücreli dışı akciğer kanseri hücrelerinde indol bileşiğinin doza ve zamana bağlı sitotoksik etki gösterdiği saptanmıştır. Saptanan kromatin kondenzasyonu, mitokondri kristalarında erime, membran undulasyonları, çekirdek parçalanması şeklinde ince yapısal değişiklikleri göstermiştir.
Sonuç: A549 hücrelerinde N,N-dimetil-4-(1-metil-3(4-nitrofenil)-1H indol-2-il) anilin bileşiğinin doza ve zamana bağlı sitotoksisitesi ve normal akciğer hücrelerinde bu etkinin daha yüksek konsantrasyonlarda görülmüş olması bileşiğin seçici antikanser etkisinin olabileceği şeklinde değerlendirilmiştir. Bileşiğin A549 hücrelerinde meydana getirdiği ince yapı değişiklikleri apoptozu indüklediğini göstermiştir. Bu bileşik yeni antikanser ajan olarak farmakokinetik ve farmasötik özellikler açısından değerlendirilmek üzere önerilmiştir.

Oral Presentation – 47

Üçlü Negatif Meme Kanseri Hücre Hattında Kuersetin ve Epigallokateşin Gallat'ın Kombine Kullanımının Doksorubisin Üzerindeki Etkinliğinin Otofaji Odaklı İncelenmesi

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Giriş ve Amaç: Üçlü negatif meme kanseri (TNBC), özellikle 45 yaş altı genç kadınlarda görülen, yüksek metastaz ve mortalite oranına sahip son derece agresif bir meme kanseri türüdür. TNBC'de ER, PR ve HER2 reseptörlerinin ekspresyonu olmadığından hedefe yönelik etkin bir tedavi yaklaşımı da bulunmamaktır. Bundan dolayı, sıklıkla ciddi yan etkileri bulunan doksorubisin gibi agresif kemoterapi ajanları ile tedavi edilmeye çalışılmaktadır. Bir hayatta kalma mekanizması olan otofaji, doksorubisine karşı kanser hücrelerinin direnç geliştirmesine neden olarak ilacın etkinliğini azaltmaktadır. Bu anlamda agresif kemoterapi ajanlarının yan etki göstermeden güvenli seviyelerde uygulanmasını ve etkinliklerinin arttırılmasını sağlayacak doğal ürünlerin kullanımına ihtiyaç vardır. Çalışmamızda, TNBC alt tipini modelleyen MDA-MB-231 hücre hattına, agresif kemoterapi ajanı olan Doksorubisin'e ek olarak daha güvenli seviyelerde uygulanmasını sağlayacak ve etkinliğini arttırması öngörülen antikanser özellikteki polifenol karışımın uygulanması amaçlanmakta olup, etkilerinin hücre canlılığına ve otofaji yolağında yer alan Beclin-1, ATG12 ve Ambra-1 anahtar genlerinin ekspresyonlarına etkisinin belirlenmesi amaçlanmıştır.

Materyal ve Metod: Bu çalışmada doksorubisin, EGCG ve kuersetin, MDA-MB-231 hücre hattına farklı dozlarda ve zamanlarda uygulanmıştır. Hücrelerin ilgili maddelere olan duyarlılığı bireysel uygulamalarla belirlendikten sonra üçlü bir karışım hazırlanmış ve kombine olarak etkileri incelenmiştir. Sitotoksisiteyi tespit etmek için MTT yapılmıştır. İstatistiksel analizler için, GraphPad Prism 10 kullanılarak iki yönlü bir anova testi uygulandı. 0,05'ten küçük P değerleri anlamlı kabul edildi. Otofaji yolağında yer alan genlerin ekspresyonel değişimlerini incelemek amacıyla RT-PCR analizi gerçekleştirilmiştir.

Sonuçlar: Karışımın, bireysel ve ikili uygulamalardan daha etkili olduğu ve anlamlı sitotoksik etkisi 48. saatte %40'lık dozdan itibaren, 72. saatte ise %25'lik dozdan itibaren görülmüştür. Çalışmamızda, ATG-12 ekspresyonu tüm tedavi gruplarında azalırken, Beclin-1 ekspresyonu kontrole göre 4 kat artış göstermiştir. Ambra-1 ekspresyonu ise doksorubisin tedavisi sonrası kontrole göre azalış gösterirken, üçlü karışımın %40 dozunda kontrole göre iki kat artış göstermiştir. Üçlü karışımın %25 dozunda ise tamamen baskılandığı gözlemlenmiştir.

Tartışma: Uygulanan karışımın, MDA-MB-231 hücre hattında otofaji yolağı üzerinde etkisi olduğu ve karışımın kanser tedavisinde etkin ve/veya tamamlayıcı bir yaklaşım olabileceği görülmüştür.

Anahtar Kelimeler: Polifenolik bileşikler, meme kanseri, otofaji

Oral Presentation – 48

In Silico Investigation of AS1411 Aptamer Variants: Structural Optimization for Enhanced Nucleolin Binding

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Aptamers are short, single-stranded DNA or RNA oligonucleotides that selectively bind to target molecules with high specificity and affinity. AS1411 is a G-rich DNA aptamer that has shown potential in targeted cancer therapy due to its strong interaction with nucleolin, a protein overexpressed on the surface of cancer cells [1]. Our study aims to explore alternative conformations of AS1411 through systematic *in silico* mutagenesis followed by the structural modeling, and thereby focusing on the thermodynamically favorable variants.

A total of 78 single and 6 double nucleotide mutations were introduced into the wild-type AS1411 sequence (26-mer) by systematically mutating each base to the other three possible bases. Secondary structure prediction was performed using the UNAfold tool, while 3D structure modeling was performed using the Xiao Lab 3dRNA/DNA Web Server. The energy values of these variants were analyzed to evaluate their thermodynamic stability, based on the principle that lower energy values indicate increased conformational robustness. Among the sequences evaluated, several mutations, such as G2C and G2C+T6C, exhibited lower energy scores compared to native AS1411, suggesting a potential improvement in their structural stability.

These findings provide a basis for further experimental validation and molecular dynamics simulations, contributing to the rational design of next-generation aptamer-based therapeutics with enhanced nucleolin binding properties.

Key words: AS1411, Aptamer, Nucleolin, In Silico Mutagenesis, Structural Modeling

1. Bates, P.J., et al., *Discovery and development of the G-rich oligonucleotide AS1411 as a novel treatment for cancer.* Experimental and Molecular Pathology, 2009. 86(3): p. 151-164.

Oral Presentation – 49

Anticancer Activity of Natural Form and Heat-Treated Form of *Arum maculatum L.* (Tirşik)

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Introduction and Aim: Hepatocellular carcinoma (HCC), which has a heterogeneous and aggressive phenotype, is the third leading cause of cancer-related deaths worldwide. HCC cases are usually diagnosed in late stages, and overall survival rates are poor. Medicinal plants with high efficacy and fewer side effects have an important place in cancer treatment, with their contents that help discover new active substances against cancer. *Arum maculatum L.* is a rich source of important chemical components. The plant, which has a poisonous effect when consumed fresh, is used to treat diseases after prolonged boiling or drying. Therefore, care should be taken when using the plant. Boiling and consuming the plant leaves is used by local people as a supplement in cancer treatment. The data obtained as a result of our study also show that *A maculatum L.* inhibits cancer progression.

Materials and Methods: Cell viability (MTT) analysis was performed to evaluate the anticancer effect of *A maculatum L.* in HepG2 and HUVEC cell lines and to compare its effects on cancer and healthy cells. HepG2 and HUVEC cell lines were treated with natural (Td) and heat-treated (T1) *A maculatum L.* plant extract for 24 hours and at different concentrations (31.25-1000 mg/mL) to evaluate percent viability.

Results: Td and T1 extracts were observed to have higher biocompatibility against healthy cells compared to cancer cells as a result of cell viability test. However, Td extract was observed to be more toxic compared to T1 extract.

Conclusion: Our data suggest that these extracts may serve as potential therapeutic agents in preventing cancer progression.

Key words: Anticancer activity, Arum maculatum L., Hepatocellular carcinoma

Oral Presentation – 50

Kanser Yaralarının Tedavisinde Kullanılmak Üzere Antimikrobiyal Sistein-Gümüş Nanopartiküllü Hidrojel Üretimi ve uygulaması

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Giriş ve Amaç: Kanser, dünya genelinde önde gelen ölüm nedenlerinden biri olmaya devam etmekte ve mevcut tedaviler, özgüllük eksikliği, yan etki ve ilaca karşı direncin ortaya çıkması nedeniyle engellenmektedir. Kendine özgü üç boyutlu yapısı, hidrofilik doğası ve biyouyumluluğu ile karakterize edilen AgNP içeren hidrojeller, hassas ilaç dağıtımı için gelişmiş kullanım imkanı sağlayarak, terapötik sonuçları iyileştirirken toksisiteyi en aza indirir. Gümüş nanopartikül içeren hidrojeller, özellikle kanser tedavisi ve yara onarımı gibi biyomedikal kullanım alanlarında önemli bir gelişme göstermektedir. Bu çalışmada, sağlıklı keratinosit hücre hattı üzerinde sitotoksiteyi ve antimikobakteriyel aktiviteyi incelemek için gümüş-sistein jeli hazırlanmıştır.

Materyal ve Metod: Hidrojel L-sistein, $AgNO_3$ ve jelleşmeyi başlatan bir tuzun (Na2SO4) çözeltileri bidistile su ile hazırlanmıştır. Karıştırılan çözelti 180 dakika boyunca UV lambası (360 nm dalga boyu) altında ışınlanmıştır. Hidrojelin karakterizasyonu FTIR, UV-vis, SEM ile yapılmıştır. Sistein-gümüş hidrojelin sitotoksik etkisi insan keratinosit (HaCaT) hücre hattı kullanılarak alamar mavisi yöntemiyle incelenmiştir. Ayrıca antibakteriyel özelliği gram pozitif (*E. coli*) ve gram negatif (*S. auresus*) bakteleri kullanılarak Disk Difüzyon yöntemi araştırılmıştır.

Bulgular: FTIR analizinde L-sistein 2549 cm^{-1}, 1586 cm^{-1}, 1389 cm^{-1}de üç ana karakteristik pik içemektedir. 2549 cm^{-1}de bulunan pik -SH'in L-sistein üzerindeki titreşim pikidir. Bu pik Sistein-gümüş kompozitinde görülmemektedir. Bu durum S'in Ag'nin yüzeyine bağlandığını göstermektedir. SEM görüntülerinde Sistein-Gümüş hidrojelin 3 boyutlu ağsı yapıda olduğu ve 122nm ile 173 nm boyutunda gümüş nanopartüküllerin sistein ile birleştiği görülmüştür. Antibakteriyel aktivite incelendiğinde sistein-gümüş hidrojelin 24 saat süre sonunda minimum inhibitör konsantrasyon (mik) değeri *E. coli* 8,33 için mm iken *S. aureus* için 8,44 mm olarak tespit edilmiştir. Ayrıca hidrojelin HaCaT hücreleri üzerine IC_{50} değeri 1307,0 µg/mL olarak tespit edilmiştir.

Sonuç: Elde edilen sonuçlar, geliştirilen hidrojelin insan keratinosit hücreleri için toksik olmadığını, biyomedikal alanda ve kanser tedavisinde kontrollü ilaç salım sistemlerinde kullanılma potansiyeli olduğunu göstermektedir.

Anahtar Kelimeler: Hidrojel, sistein, gümüş nanoportikül, kanser, sitotoksisite, antibakteriyel

Teşekkür: Bu çalışma Selçuk Üniversitesi Bilimsel Araştırma Projeleri (BAP) Koordinatörlüğü tarafından desteklenmiştir (Proje No:22112003).

Oral Presentation – 51

Exploring bladder, prostate, and endometrial cancer risk in RRMS patients: ATM, CREB1, and miR-19b-3p are shared biomarkers

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Introduction and Aim: Relapsing-remitting multiple sclerosis (RRMS) is the most common phenotype of MS. Bladder urothelial cancer (BLCA) is the highly prevalent malignancy of the urinary system. Prostate adenocarcinoma (PRAD) is the leading cause of cancer-related morbidity and mortality in males. Uterine corpus endometrial carcinoma (UCEC) is a prevalent malignancy within the female. Identifying the risk of BLCA, PRAD, and UCEC in RRMS patients is of critical importance. This study aims to identify potential biomarkers that pose a risk for BLCA, PRAD, and UCEC in RRMS patients and have a common role.

Materials and Methods: Expression profiles of RRMS patients were obtained from the GEO and ArrayExpress databases. Differentially expressed miRNAs (DEMs) and mRNAs (DEGs) were identified using the Principal Component Analysis (PCA)-based Unsupervised-Feature-Extraction (UFE) method. GEO2R was applied to analyze datasets, and DEGs and DEMs were classified based on fold change. Target genes of up/downregulated DEMs were identified, and common gene clusters with corresponding up/downregulated DEGs were determined. Further bioinformatics analyses were conducted to identify hub-miRNAs and hub-genes.

Results: 321 control and 293 RRMS samples were analyzed. DEMs and DEGs were identified using both the PCA-based UFE and GEO2R, and their intersections were determined. Target genes of DEMs were selected based on validation and prediction in at least two databases. Negatively correlated target genes of up/downregulated DEMs were identified, and common gene clusters were established. STRING analysis was performed, and negative regulatory network was constructed using Cytoscape. Validation of hub-genes and hub-miRNAs in BLCA, PRAD, and UCEC was conducted using UALCAN and OncomiR.

Discussion: Decreased ATM and CREB1 have been identified as direct targets of hsa-miR-19b-3p. They were identified as potential biomarkers in RRMS and further validated in BLCA, PRAD, and UCEC. This study highlights biomarkers in RRMS patients that may contribute to an increased risk of these cancers.

Key words: RRMS, BLCA, PRAD, UCEC, biomarker

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Oral Presentation – 52

A Pyroptosis-Related lncRNA Signature in Papillary Thyroid Cancer: Prognostic, Immunological, and Therapeutic Perspectives

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Introduction and Aim: While expanding evidence suggests that long non-coding RNAs (lncRNAs) are critical in competing endogenous RNA (ceRNA) networks, the involvement of pyroptosis-associated ceRNA (PRceRNA) networks in papillary thyroid carcinoma (PTC) and their prognostic potential remain unexplored. In this study a novel risk signature model for pyroptosis-related lncRNAs (PRlncRNAs) was created to predict clinical outcomes in PTC. A nomogram by integrating risk score (RS) with clinical factors was built to evaluate survival prediction.

Materials and Methods: TCGA database was utilized to acquire miRNA, transcriptome sequencing, and clinical data. DEmiRNAs, DEmRNAs, and DElncRNAs were specified and used to establish a PRceRNA network. The dataset was divided into training and test sets randomly. First, a PRlncRNA risk model was built using univariate Cox and LASSO regression analysis on the training set. Then the prognostic signature was assessed through survival and ROC analyses. Then the signature was validated in the testing and entire sets through univariate and multivariate Cox regression analysis and nomogram-based prognostic evaluation. Finally, the association between the risk model and tumor-infiltrating immune cells via ESTIMATE and CIBERSORT algorithms and chemotherapy drug sensitivity analysis via Genomics of Cancer Drug Sensitivity database was examined.

Results: A prognostic signature composed of six-lncRNAs (AC007365.1, AC133785.1, AC134682.1, AP000462.1, AL049712.1, and AC018685.2) was constructed. Patients were divided into high-risk (HR) and low-risk (LR) groups according to the median risk score. Kaplan-Meier survival analysis exhibited significantly shorter survival in the HR group. ROC analysis, univariate/multivariate Cox regression analyses, and nomogram evaluation confirmed that the risk model was an independent prognostic factor with strong predictive performance. Furthermore, immune infiltration was significantly increased in the LR group. Drug sensitivity analysis identified four potential therapeutic agents (Trametinib, AZD5582, Dihydrorotenone, and BMS.754807) for HR and LR patients.

Discussion: This study provides a new risk model to assess PTC prognosis and potential therapeutic targets associated with pyroptosis.

Key words: Papillary thyroid cancer, pyroptosis-related genes, lncRNA, immune microenvironment, ceRNA regulatory network

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Oral Presentation – 53

Investigation of the Functional Role of Complement System Protein, C4BPB, as a Candidate Oncogene in TNBC

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Introduction and Aim: Breast cancer is the most common cancer among women, and its heterogeneous nature poses significant treatment challenges. Triple-Negative Breast Cancer (TNBC), characterized by the absence of hormone receptors and its aggressive clinical behavior, has the poorest prognosis. This study aims to identify and functionally characterize candidate oncogene in chromosome 1q, associated with transcriptional upregulation in TNBC.

Materials and Methods: We conducted a bioinformatic analysis focusing on gene expression in TNBC cell lines using three publicly available RNA-seq datasets. The CRISPR-Cas9 system was employed to knockout the candidate gene in MDA-MB-231 cells, generating stable knockout cell lines. The effects of gene deficiency on proliferation, growth rate, colony formationS, and cell cycle progression were evaluated using competition assays, MTT assays, colony formation assays, and cell cycle analysis. Cyclin and CDK gene and protein levels were analyzed via RT-qPCR and Western blotting to explore cell cycle regulation.

Results: We identified 63 significantly upregulated genes (p < 0.05 and fold-change > 2) in TNBC cell lines. Notably, C4BPB was significantly upregulated in MDA-MB-231 cells, making it a candidate for further study. RT-PCR confirmed the upregulation of C4BPB in TNBC cells. C4BPB knockout led to reduced cell proliferation, colony formation, and alterations in the cell cycle, with a G1 phase arrest.

Discussion: The oncogenic role of C4BPB in breast cancer highlights its potential as a prognostic biomarker and a therapeutic target. Further investigations into the interaction between cell cycle proteins and C4BPB will enhance our understanding of its function in breast cancer progression. Moreover, transcriptomic analyses of C4BPB-deficient cells may reveal differentially expressed genes and disrupted biological pathways, underscoring the significance of the complement system in cancer therapy.

Key words: Oncogene, TNBC, Bioinformatics, Cell Cycle

Oral Presentation – 54

The Involvement of AP-1 Target Transcript VAV3.1 in Osimertinib Resistance in Lung Adenocarcinoma

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Introduction and Aim: Lung adenocarcinoma is a highly lethal cancer, frequently driven by EGFR mutations. Although osimertinib is the most effective FDA-approved EGFR-TKI, resistance inevitably develops. To explore resistance mechanisms, we performed a CRISPR knockout screen that identified the AP1 transcription factors FOSL1 and JUN as key modulators of osimertinib resistance. Silencing either gene restored drug sensitivity, revealing a synthetic lethal interaction with the EGFR pathway. Multi-omics analyses (RNA-Seq, ATAC-Seq, CRISPR screen) further implicated VAV3.1—a distinct transcript of VAV3—as a resistance-associated gene.

Materials and Methods: To investigate the role of VAV3.1, we combined bioinformatic analyses with in vitro experiments. We validated VAV3.1 as the dominant isoform in HCC827- OsiR cells using qRT-PCR and RNA-Seq. CRISPR-Cas9 knockout and shRNA knockdown were used to assess its role in resistance via 2D colony formation, western blotting, BrdU, and competitive proliferation assays. VAV3.1 was overexpressed in parental HCC827 cells to evaluate its effect on proliferation.

Results: Our findings confirmed that VAV3.1, distinguished by a unique 110-nucleotide sequence suggesting distinct promoter regulation, is the predominant VAV3 transcript in our cells. Multi-omics analyses revealed notable changes in expression and chromatin accessibility, supporting its role in resistance. CRISPR-mediated knockout had a minor effect, while shRNA- mediated knockdown led to more consistent sensitization to osimertinib.

Discussion: Here, we present the first preliminary findings of VAV3.1 as a potential downstream effector of the AP1 family in mediating resistance to osimertinib. These findings underscore the complexity of transcript-specific resistance mechanisms. Ongoing studies aim to clarify VAV3.1's function and therapeutic potential.

Key words: CRISPR/Cas9, osimertinib, resistance, vav3.1, NSCLC

Oral Presentation – 55

Genome-Wide CRISPR Screening Reveals RUVBL1/2 as a Therapeutic Target in Bladder Cancer

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Introduction and Aim: Bladder cancer is a prevalent urological malignancy with high recurrence rates and limited treatment options, highlighting the need for novel therapeutic targets and biomarkers. The RUVBL1/2 complex, composed of the AAA+ ATPases RUVBL1 and RUVBL2, regulates key cellular processes and has been implicated in various cancers. Inhibition of RUVBL1/2 has been shown to reduce tumorigenic features in several cancer types. However, its specific role in bladder cancer remains unclear. This project aims to elucidate the molecular and cellular functions of RUVBL1/2 in bladder cancer, assess its druggability via CRISPR/Cas9 or pharmacological approaches, and evaluate its biomarker potential.

Material and Method: A genome-wide CRISPR/Cas9 screening using the Brunello library was conducted in J82 and RT4 bladder cancer cell lines, followed by bioinformatic analyses and initial validations in a panel of cell lines. This approach identified RUVBL1 and RUVBL2 as druggable vulnerabilities in bladder cancer. To explore the role of the RUVBL1/2 complex, extensive cellular and molecular analyses were performed in RUVBL1/2-depleted cells using CRISPR/Cas9 or pharmacological inhibition. Functional assays included proliferation, BrdU incorporation, cell cycle and apoptosis, clonogenic and 3D anchorage- independent growth, migration, invasion, and DNA damage assessments. Pharmacological inhibition further validated the therapeutic relevance of RUVBL1/2, supporting its potential as a novel target in bladder cancer.

Results: Genetic depletion or pharmacological inhibition of the RUVBL1/2 complex using the selective inhibitor CB-6644 significantly impaired key cancer cell functions, including proliferation, survival, and anchorage-independent growth. Treated cells exhibited cell cycle arrest and increased apoptosis. Additionally, RUVBL1/2 expression was elevated in bladder tumors and associated with shorter overall survival, highlighting its therapeutic relevance.

Discussion: Our findings reveal bladder cancer's critical dependency on the RUVBL1/2 complex, underscoring its potential as both a biomarker and a therapeutic target. Further investigations into its cellular and molecular interactions will provide deeper insights into the functional role of RUVBL1/2 in bladder cancer progression.

Key words: Bladder Cancer, RUVBL1/2, CRISPR/Cas9, Pharmacological Inhibition

Oral Presentation – 56

ATPase-Dependent Oncogenic Role of RUVBL1/2 Overexpression in Bladder Cancer

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Introduction: Bladder cancer is a common urological malignancy with high recurrence rates and limited treatment options, emphasizing the need for new therapeutic targets. The RUVBL1/2 complex, composed of the AAA+ ATPases RUVBL1 and RUVBL2, regulates essential cellular processes like chromatin remodeling and DNA repair. Although its dysregulation is linked to various cancers, its role in bladder cancer is not well defined. This study investigates whether overexpression of RUVBL1/2 contributes to bladder cancer progression and whether this effect depends on its ATPase activity. Understanding this mechanism could highlight the therapeutic potential of targeting the complex.

Materials and Methods: In our previous work, a genome-wide CRISPR/Cas9 screen identified RUVBL1 and RUVBL2 as vulnerabilities in bladder cancer, confirmed by genetic knockout and inhibitor studies. Building on these findings, we overexpressed wild-type and ATPase-dead mutant forms of RUVBL1/2 in RT4, RT112, and J82 bladder cancer cell lines. Functional assays included 2D colony formation (CF) to assess proliferation, immunofluorescence (IF) to detect subcellular localization, and 3D soft agar assays to evaluate anchorage-independent growth.

Results and Discussion: Overexpression of wild-type RUVBL1/2 significantly increased proliferation and colony formation in all three cell lines, whereas ATPase-dead mutants showed reduced effects. This indicates that ATPase activity is crucial for the oncogenic functions of RUVBL1/2 in bladder cancer. While these findings support its functional relevance, ongoing experiments are investigating a potential connection between RUVBL1/2-driven proliferation and epithelial-mesenchymal transition (EMT).

Conclusion: These results demonstrate that RUVBL1/2 overexpression promotes bladder cancer cell proliferation through an ATPase-dependent mechanism. The reduced tumorigenic potential of ATPase mutants highlights this domain as a promising therapeutic target in bladder cancer.

Key words: Bladder cancer, Ruvbl1/2, EMT

Oral Presentation – 57

Regulatory Variations in Oligodendrogliomas: A Targeted Approach to 1p and 19q Genomic Alterations

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Introduction and Aim: Oligodendrogliomas (OGs) account for ~5-10% of all gliomas, which are generally associated with favorable prognosis, improved treatment responses, and longer survival (1). They are classified based on their molecular characteristics, particularly *IDH* mutations and the co-deletion of chromosomal arms-1p and 19q (2,3). Other genetic alterations including *CIC* and *TP53* mutations are less common (1,4). Since potential alterations in other genes remain unknown, our goal is to investigate novel or notable genetic variations on chromosome 1p and 19q, particularly in regulatory regions that may impact disease diagnosis, prognosis, and treatment.

Materials and Methods: Targeted sequencing was conducted using the HiSeq 2500 platform with 2x100 bp read configuration. The study included one healthy brain tissue and 15 OG patient tumors, all of which underwent targeted capture for all genes on 1p and 19q regions. A -650 bp region was extended, and a +250 bp region was added to the first exons, allowing the target area to encompass regulatory elements as promoters and transcription factor (TF) binding sites.

Results: Variant reports were generated by filtering raw mutation data, yielding an overall alignment rate of 92%. A total of 150,599 variants were identified, differing from the control with *ZNF* families, *GP6* and *PSG3* genes being the most prevalent. Notably, 203 intronic variants in endothelin-converting enzyme-1 *(ECE1),* a gene potentially linked to cancer invasiveness and poor prognosis recently (5) were

detected in all patients. A key variant, rs3026809 was identified in 7/15 OG patients (Sanger-sequencing confirmed) remarkable for its proximity to predicted TF-binding sites.

Despite its high allele frequency in gnomAD, CADD and LoFtool scores are noteworthy. Discussion: Intronic variants are increasingly recognized in the molecular mechanisms of gliomas. These findings offer valuable insights, yet further investigation involving comprehensive sequencing techniques with larger sample sizes or different glial tumors, along with collaborative multi-omics and functional studies, will strengthen the research impact.

Key words: Glial Tumors, Oligodendroglioma, Targeted Sequencing, 1p19q co-deletion, ECE1

References (if any):

1. Tork CA, Atkinson C. Oligodendroglioma. [Updated 2025 Jan 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559184/

2. Xia, Y., Yang, F., Wang, Y., Wang, Y., Wang, Y., Dai, C., … & Zhao, B. (2022). Molecular landscape of idh-mutant astrocytoma and oligodendroglioma grade 2 indicate tumor purity as an underlying genomic factor. Molecular Medicine, 28(1). https://doi.org/10.1186/s10020-022-00454-z

3. de la Fuente, Macarena I. "Adult-type diffuse gliomas." *CONTINUUM: Lifelong Learning in Neurology* 29.6 (2023): 1662-1679. https://doi.org/10.1212/con.0000000000001352

4. Roberto K, Lim-Fat MJ. Circulating biomarkers in diffuse gliomas: current landscape and future directions. Practical Neurology (US). 2024;23(2):44-48.

5. Tapia JC, Niechi I. Endothelin-converting enzyme-1 in cancer aggressiveness. Cancer Lett. 2019 Jun 28;452:152-157. doi: 10.1016/j.canlet.2019.03.033. Epub 2019 Mar 26. PMID: 30926432.

Oral Presentation – 58

Üçlü negatif meme kanserinde AXL hedeflenmesi ve Amuvatinib'in etkileri: miRNA-3142 ile miRNA-5687 ifadelenmesi ön sonuçlar

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Giriş ve Amaç: AXL, reseptör kinazlardan TAM (Tyro3, AXL ve MER) ailesinin önemli bir üyesidir. AXL, uzun yıllar gizemini korumuş olsa da moleküler düzeyde kanser çalışmalarının ilerlemesi ile farklı bir bakış açısı kazanmıştır. AXL, Üçlü negatif meme kanserinde (TNBC) proliferasyonu, sağkalımı, invazyonu ve göçü artırarak kanser gelişimini destekleyen aynı zamanda tedavilerde direnç gelişmesine neden olan bir onkogendir. FDA onaylı AXL'i hedefleyen ilaçların varlığı AXL'nin tedaviye direnç gelişimindeki rolünün anlaşılması, yeni kanser terapötik stratejilerin geliştirilmesi için bir ışık tutabilir. Bu çalışma TNBC tedavisinde kullanılan kemoterapik ajan Amuvatinib'in etki mekanizmasında bazı miRNA'ların nasıl ifadelendiğini belirlemek amacıyla planlanmıştır.

Materyal ve Metot: Docing testi ile TNBC tedavisinde kullanılan ve AXL geni bağlanma kapasitesi en yüksek kemoterapötik ajan tirozin kinaz inhibitörü Amuvatinib olarak tespit edildi (docing score: -7.054). Amuvatinib'in; TNBC hücre hattı olan MDA-MB-231 hücrelerinde etkin dozu MTT assay testi ile belirlendi. TNBC hücre hattında AXL genini hedefleyen miRNA'ları belirlemek için miRPathDB 2.0 database kullanıldı. Hedef genlerimizin ifadelenme düzeyleri ise qPCR aracığıyla değerlendirildi.

Sonuçlar: Çalışmamızın sonucunda Amuvatinib'in (tirozin kinaz inhibitörü) AXL geninin aktivasyonunu artırarak kötü prognoza neden olduğu bulunmuştur (*p<00,273). AXL genini hedefleyen ilgili miRNA'lar (miR-3142 ve miR-5687) düzeyinde anlamlı bir ekpresyon artışı veya azalışı gözlenmemiştir. Casp8 etkin doz (IC50) üzerinde anlamlı ekpresyon artışı gözlenmiştir (*p=0,0510). İleriki tetkikler devam etmektedir.

Tartışma: TNBC tedavisinde, Amuvatinib'in tedaviye dirençte önemli rolü olan AXL geninin ifadelenmesini artırdığını ve hücre ölümünün apoptoz markırları üzerinden gerçekleşmediğini belirledik. İleri tetkikler devam etmektedir.

Anahtar Kelimeler: AXL, TNBC, miRNA-3142, miRNA-5687, Amuvatinib.

Oral Presentation – 59

TLR3 Stimulated Mesenchymal Stem Cells Regulate Antitumor Responses of Pancreatic Adenoductal Carcinoma Cells

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Introduction and Aim: Pancreatic cancer is low survival rates and high metastatic potential. One of the main reasons for treatment failure is the dense desmoplastic microenvironment of the tumor. Mesenchymal stem cells(MSCs) can affect the tumor microenvironment by secreting molecules. While some studies suggest that MSCs have antitumorigenic effects, others suggest that they may promote tumor progression. In this study, we investigate the effects of both naïve MSCs and TLR3-induced or inhibited MSC phenotypes on apoptosis, cell cycle and expression of tumor-associated genes in Panc-1 cells.

Materials and Methods: Adipose-derived MSCs were treated with a TLR3 agonist(0.5 μg/ml) and antagonist(1 μg/ml) based on cytokine (IL-6, TNF-α, IL-1β, IL-1α, IL-10, and TGF-β) gene expression responses. In an indirect co-culture model using 0.4 μm inserts, Panc-1 cells were cultured with MSCs at a 1:10 ratio. Apoptosis, cell cycle, and gene expression analyses were performed at 72 hours.

Results: At the end of 72h, apoptosis was highest in the TLR3-stimulated MSC-Panc-1 group(44%) and lowest in the Panc-1 group (25%). The percentage of cells in the G1 phase increased in the naïve(61.4%) and TLR3-stimulated MSC-Panc-1 groups(61.8%) compared to the Panc-1 group(51.6%). In naïve and TLR3-stimulated MSCs, CD44, ZEB1, and VIM expression in Panc-1 cells was downregulated, while CDH1 and CLDN1 were upregulated. MMP2 and MMP9 were downregulated in all groups, whereas TIMP1, PLAU, and VEGFR2 were upregulated.

Discussion: The effects of MSCs on cancer cells remain controversial in the literature. Pro-inflammatory MSCs (MSC1) have been shown to have antitumor properties and anti-inflammatory MSCs (MSC2) have been shown to have protumor properties. However, in co-culture studies, this effect was most pronounced at a ratio of (Panc-1)10:1(MSC). Understanding the role of MSCs in the tumor microenvironment will provide insights for the development of future microenvironment-targeted therapeutic approaches.

Key words: Pancreatic cancer, Mesenchymal stem cells, TLR3, tumor microenvironment, MSC2.

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Oral Presentation – 60

In vitro and in vivo evaluation of the effects of eEF2 kinase inhibition on cell death mechanisms in triple negative breast cancer

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Introduction and Aim:Deregulation in apoptosis has observed in many cancers including triple negative breast cancer (TNBC). This situation causes mechanisms such as autophagy to be targeted in studies. Autophagy functions depending on the type and stage of cancer. eEF2K plays an important role in the regulation of autophagy and apoptosis in cancer and highly expressed in TNBC. Rottlerin is a polyphenolic compound which inhibits eEF2K. We hypothesized that Rottlerin enhances apoptosis through autophagy activation in TNBC and we aimed to evaluate the effectiveness Rottlerin on autophagy and apoptosis in vitro and in vivo.

Materials and Methods:4T1were treated with Rottlerin and autophagy regulation was assessed with LC3A/B staining. Cells were treated with Rottlerin in combination with autophagy inhibitor to reveal the role of autophagy. Autophagy regulator proteins p-ERK and p-mTOR were evaluated by IF staining.For in vivo experiments, 1x106 cells were orthotopically injected into Balb/C mice and the animals were divided into six groups regarding Control, 4T1, 4T1+DMSO, 4T1+ROT(Rottlerin), 4T1+DOX(doxorubicin) and 4T1+ROT+DOX. At 4 th week, primary tumor and metastatic tissues were excised, analyzed and LC3A/B, active- caspase-3, p-ERK and p-mTOR expressions were evaluated.

Results:Rottlerin enhanced LC3A/B protein expression while reduced the p-ERK and p- mTOR. Rottlerin-mediated apoptosis were reduced by autophagy inhibition in 4T1 cells. In in vivo experiments, we observed enhanced tumor weight and micro-metastasis in 4T1 while 4T1+ROT, 4T1+DOX and 4T1+ROT+DOX have reduced tumor weight and metastatic lesions(*$p<0,05$). In primary tumors, increased p-ERK and p-mTOR expressions were observed in 4T1 and these were reduced with Rottlerin. Rottlerin increased LC3A/B and active-caspase- 3 expression(*$p<0,05$).

Discussion:Although it is known that eEF2K regulates autophagy in cancer, the effect of Rottlerin on autophagy regulation in TNBC has not yet known. Our study shows that TNBC progression is restricted by eEF2K inhibition-mediated autophagy activation and apoptosis, will also lead to similar studies in different types of cancer.

Keywords:TNBC, Rottlerin, cell death

Oral Presentation – 61

MiR-99b-5p Modulates Apoptosis in Breast Cancer by Targeting the TRAIL-R/DR5/BAK Axis: Insights from AGO2-RIP-Seq and In Vivo Models

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Introduction and Aim: Dysregulation of microRNAs plays a crucial role in breast cancer pathogenesis, yet the functional contributions of many miRNAs remain unclear. In this study, we identified miR-99b-5p as an oncogenic microRNA, with its upregulation in breast tumors confirmed through The Cancer Genome Atlas (TCGA) data analysis. Our in-vitro studies demonstrated that miR-99b-5p downregulation in triple-negative breast cancer (TNBC) cells significantly decreased cell proliferation, primarily through the induction of apoptosis. Building on these findings, we sought to identify the direct targets of miR-99b-5p and further investigate its functional significance in breast cancer.

Materials and Methods: miR-99b-5p's direct targets were identified through AGO2-RNA immunoprecipitation followed by high-throughput sequencing (AGO2-RIP-Seq). Stable miR-99b-5p knockdown was established in MDA-MB-231 cells, and xenograft models were generated in nude mice to explore miR-99b-5p's functional role in vivo. To assess the underlying molecular mechanisms qRT-PCR, Western blot analysis and luciferase reporter assays were performed.

Results: AGO2-RIP-Seq analysis revealed that miR-99b-5p regulates genes involved in apoptosis, cell cycle control, and ubiquitin-mediated protein degradation. Knockdown of miR-99b-5p suppressed MDA-MB-231 cell growth and elicited significant tumor regression in orthotopic tumor-bearing mice. Mechanistically, RIP-Seq data and molecular assays demonstrated that miR-99b-5p suppression induces apoptosis through activation of the TRAIL-R signaling pathway via the miR-99b-5p/DR5/BAK axis, as confirmed by qRT-PCR and Western blot analysis. Luciferase reporter assays confirmed DR5 as a direct target of miR-99b-5p.

Discussion: These findings establish miR-99b-5p as a critical regulator of apoptosis in breast cancer and highlights its therapeutic potential. The characterization of its targetome provides novel insights into breast cancer biology, offering a foundation for potential miRNA-targeted therapeutic strategies.

Oral Presentation – 62

Effect of the Lichen-Derived Compound Usnic Acid on Endoplasmic Reticulum Stress (ERS) Modulation in Colorectal Cancer Cells

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Introduction and Aim: Usnic acid, a secondary metabolite derived from lichens, is a compound of increasing interest due to its notable anti-tumoral and cytotoxic properties. Endoplasmic reticulum (ER) stress plays a critical role in pathophysiological conditions such as cancer, where cellular homeostasis is disrupted. ER stress influences whether tumor cells undergo apoptosis or continue to survive under unfavorable conditions (1). Colorectal cancer (CRC) ranks as the second leading cause of cancer-related deaths and is the third most common type of cancer worldwide (1; 2). This study aims to investigate the modulatory effect of usnic acid on ER stress in colorectal cancer cells, providing new insights into how usnic acid may regulate cellular responses linked to ER stress.

Materials and Methods: In this study, the effect of usnic acid on ER stress was evaluated in HT-29 colorectal cancer cells. HT-29 cells were treated with different concentrations of usnic acid, and changes associated with ER stress were analyzed. Protein lysates were collected from the cells, and Western blot analysis was performed to detect ER stress markers. Specifically, the expression levels of ATF6 and IRE1α proteins were assessed. Cell viability in response to usnic acid treatment was determined using the MTT assay.

Results: The results indicated that treatment with selected concentrations of usnic acid increased the expression levels of ER stress markers in HT-29 colorectal cancer cells. Additionally, alterations in cell viability were observed across different treatment groups.

Discussion: This study demonstrated that usnic acid induces ER stress in HT-29 colorectal cancer cells and reduces cell viability. The observed increase in the expression of ER stress-related proteins following usnic acid treatment suggests that apoptotic pathways may be activated. Previous studies have reported the anti-tumoral and pro-apoptotic effects of usnic acid in various cancer cell lines (1). Our findings support a similar mechanism in colorectal cancer cells. Overall, the results suggest that usnic acid may serve as a potential adjuvant agent in colorectal cancer therapy by targeting ER stress pathways. Further in vivo studies are necessary to validate these effects and to elucidate the detailed molecular mechanisms involved.

Key words: Colorectal cancer; Lichen; Usnic acid; Endoplasmic reticulum stress

References:

1. Pyrczak-Felczykowska, A., Reekie, T. A., Jąkalski, M., Hać, A., Malinowska, M., Pawlik, A., … & Herman-Antosiewicz, A. (2022). The isoxazole derivative of usnic acid induces an er stress response in breast cancer cells that leads to paraptosis-like cell death. International Journal of Molecular Sciences, 23(3), 1802. https://doi.org/10.3390/ijms23031802

2. Xi, Y., & Xu, P. (2021). Global colorectal cancer burden in 2020 and projections to 2040. *Translational oncology*, *14*(10), 101174.

Oral Presentation – 63

Boric Acid-Mediated Changing of Macrophages Plasticity

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Introduction and Aim: Boric acid (H3BO3) is the most common form of boron and has a protective role in the body from oxidative stress as it can inhibit the production of reactive oxygen species. Boron protects bone health by increasing bone cell proliferation, survival, mRNA expression and mineralization. The studies have been reported improvements in individual measures of limited movement, pain relief, and joint swelling in arthritic individuals receiving boron. Boron acts as an inflammatory agent through various immune pathways and creates an immune response. This study aimed to investigate the effect of boric acid on the inflammatory response in murine macrophage cells.
Materials and Methods: Boric acid's cytotoxic effect on the murine macrophage cell line RAW264.7 cells was examined using MTT assay. Different concantrations of boric acid (50, 250, 1250, 2500, 5000, 15000, and 25000 μM) were administered. RNA isolation was carried out after the IC50 dose was determined. qRT-PCR was used to analyze the genes linked to inflammation that are involved in macrophage activation.
Results: The IC50 doses of boric acid were calculated as 14.4 mM. As a result of gene expression analysis, expression of CD86, IL1B, IL6, TNFR1, TNFR2, TCFB, STAT3 and STAT6 increased significantly ($p<0.05$) and expression of MCP-1 increased insignificantly ($p>0.05$) in boric acid-treated macrophage cells. Expression of CD163, IL4, IL10 and STAT1 decreased significantly ($p<0.05$).
Discussion: Boric acid has been shown to change the inflammatory tendency in murine macrophage cells by gene expression analysis. Boric acid applied macrophage cells exhibited a gene expression profile towards M1 type.
Key words: Boric acid, macrophage, inflammation

Oral Presentation – 64

Reviving the Classics: Venetoclax Sensitizes Lung Cancer Cells to Conventional Chemotherapeutics via Ferroptotic Pathways and DNA damage

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Introduction and Aim: Venetoclax is a trending Bcl-2 inhibitor approved by FDA for chronic lymphocytic leukemia. However, its potential benefit in different type of cancers remains unclear. In the present study, conventional chemotherapeutics (etoposide and cisplatin) were combined with venetoclax and their synergistic activity was investigated in non-small cell lung cancer cells as well as their underlying mechanisms.

Materials and Methods: Human non-small cell lung cancer cells (A549) and normal cells (L929) were treated with single etoposide, cisplatin, venetoclax for 24 and 48 h. Then, venetoclax (8 μM) was co-treated with etoposide and cisplatin in various concentrations for 24 h and the viable cells were detected with MTT test. DCFH-DA staining was used to monitor ROS generation, calcein and neutral red staining were carried out for iron and lipid accumulation and visualized by confocal microscopy. TBARS assay was performed to measure lipid peroxidation levels and RT-qPCR was used to analyse ferroptotic gene expressions.

Results: MTT analyses demonstrated significant synergism between venetoclax (8 μM) and etoposide (16 μM), while no significant change was observed in cisplatin treatment group. Cell viability rates were 82.18±2.59% and 81.38±2.96% in single treatments and 64.48±0.87% in combination treatment. Furthermore, TBARS assay indicated significantly increased lipid peroxidation by 51%, which was supported by remarkably enhanced ROS generation, iron and lipid accumulation according to confocal microscopy assays. Additionally, gene expression analyses revealed 2-fold increase in transferrin gene expression in combination treatment, while no significant change was detected in single treatments. Finally, DNA damage marker H2AX was upregulated by 2.5-fold compared to single etoposide treatment.

Discussion: Data of the present study revealed for the first time that etoposide in combination with venetoclax induces ferroptotic pathways as well as DNA damage in lung cancer cells.

Key words: Cisplatin, etoposide, ferroptosis, lung cancer, venetoclax.

Oral Presentation – 65

Uncovering A Novel Mechanism of Cucurbitacin B: Short-Term Exposure Demonstrates Disulfidptosis-Like Cell Death in Lung Cancer Cells

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Introduction and Aim: Disulfidptosis is a newly identified cell death mechanism which involves cysteine deprivation and altered cytoskeletal markers. Cucurbitacin B (CuB) is a plant-derived triterpenoid with potent antitumor activity. Various pathways were reported regarding its mechanism; however, there is limited data on its short-term effect as well as the post effect of the compound.

Materials and Methods: A549 lung cancer cells and L929 healthy cells were administered with CuB for 2 hours, then it was replaced with fresh medium for recovery. Post effect of the compound was monitored in a time-dependent manner in the presence or absence of n- acetylcysteine, glutathione, ferrostatin-1, trolox, histidine and cysteine. Cytotoxicity was determined with MTT assay. ROS generation was detected with confocal microscopy. Lipid peroxidation was measured with MDA assay. Gene expression analyses were carried out with RT-qPCR.

Results: Results indicated that following only 2-hour exposure to CuB, cell viability went down to 63.44±1.69% after 24 hour and 49.51 ± 0.79% after 48 hour in fresh medium, displaying sustained cytotoxicity. In contrast, L929 cells were not affected by the same treatment, where cell viability remained 91.70±1.44% even after 48 hour. Confocal microscopy revealed increased ROS generation, leading to enhanced lipid peroxidation by 58.74±6.33%. Further analysis demonstrated that only n-acetylcysteine, glutathione and cysteine reverse the observed toxicity, indicating the involvement of cysteine deprivation. Additionally, RT-qPCR analysis indicated upregulated SLC7A11 expression in CuB-treated cells. NCKAP1 expression, a marker for cytoskeleton formation, was altered by 3-fold and DNA damage marker H2AX expression was upregulated by 2-fold.

Discussion: The present study demonstrated for the first time that only 2-hour treatment of CuB leads to selective and sustained cytotoxicity in lung cancer cells even after 48h via disulfidptosis-related pathways, indicating a novel potential of the compound in treatment.

Key words: Cucurbitacin B, disulfidptosis, lung cancer.

Oral Presentation – 66

Spontaneous Differentiation and Autophagy Modulation in Caco-2 and T84 Colorectal Cancer Cells

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Introduction and Aim: CaCo-2 and T84 colorectal cancer (CRC) cells serve as models for intestinal and colonic differentiation, respectively. Spontaneous differentiation in CaCo-2 cells is linked to autophagic flux activation[1], but its dynamics in T84 cells remain unknown. This study investigates differentiation, autophagy induction, and molecular regulators in CaCo-2 and T84 cells.

Materials and Methods: Differentiation was confirmed by tight junction formation and disruption, assessed via xCELLigence electrical impedance. Alkaline phosphatase activity was measured as a differentiation marker. Autophagy induction and flux were evaluated via western blot. Small RNA sequencing identified differentially expressed microRNAs (miRNAs), followed by gene set enrichment analysis (GSEA). Five miRNAs were selected based on predicted interactions with autophagy-regulating mRNAs. qRT-PCR validated miRNA expression, and miR-143 target verification was performed.

Results: Both cell lines showed autophagy induction during differentiation, but only CaCo- 2 maintained intact flux, while T84 exhibited impaired flux via increased p62 cargo protein accumulation. Small RNA sequencing identified 174 differentially expressed miRNAs, with GSEA highlighting autophagy-related pathways. qRT-PCR confirmed miR-143 downregulation out of 5 selected miRNAs. Pathway analysis suggested potential miRNA targets in autophagy regulation. Target verification studies indicated Rab7a as potential target of miR-143.

Discussion: Spontaneous differentiation differentially affects autophagy in CaCo-2 and T84 cells. Impaired autophagic flux in T84 may be miRNA-regulated, with miR-143 potentially influencing Rab7a and lysosomal localization. These findings highlight autophagy's role in CRC differentiation and potential therapeutic implications.

References:

1. Tunçer, S. & Banerjee, S. Determination of Autophagy in the Caco-2 spontaneously Differentiating Model of Intestinal Cells. *Methods Mol. Biol.* 257–284 (2017). doi:10.1007/7651

Oral Presentation – 67

Ferroptotik Hücre Ölümüne Yeni Bir Bakış: Nöroblastom Hücrelerinde RG7388-Erastin Etkileşimi

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Amaç: Nöral krest hücrelerinden köken alan nöroblastom, çocukluk çağının en sık görülen ekstrakranial solid tümörü olmakla birlikte yüksek riskli hastalarda mortalite oranları yüksek seyredebilmektedir. Bu nedenle yeni tedavi stratejileri geliştirilmesi, tümör hücresinin ve hücre ölüm yöntemlerinin anlaşılması, tedavi edici ajanların etki mekanizmalarının açığa kavuşturulması önem arz etmektedir. Bu çalışmada, proapoptotik p53'ü negatif yönde düzenleyen MDM2'nin yeni keşfedilmiş bir inhibitörü olan RG7388'in (idasanutlin), demir birikimi ve lipid peroksidasyonuyla karakterize edilen ferroptotik hücre ölümüne etkisinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: İnsan nöroblastom SH-SY5Y hücrelerine 10 ve 20 µM RG7388 24 saat uygulanarak hücre canlılığı MTT analiziyle değerlendirilmiştir. Ferroptoz inhibitörleri olan deferoksamin mesilat (DFOM) veya ferrostatin-1 (Fer-1) ile 3 saatlik ön muamelenin ardından aynı RG7388 dozları yeniden uygulanarak MTT testi tekrarlanmıştır. Ardından, ferroptoz indükleyici ajan olan erastinin en düşük sitotoksik dozu MTT testiyle 400 nM olarak belirlenmiş ve RG7388 ile kombine halde uygulanmıştır. Kombinasyon gruplarına DFOM veya Fer-1 ile ön muamele uygulanarak MTT analizi gerçekleştirilmiştir.

Bulgular: RG7388'in 10 ve 20 µM dozlarında sırasıyla %83 ve %78 hücre canlılığı gözlenmiştir. Fer-1 ön muamelesi sonrası bu oranlar %86 ve %69, DFOM ön muamelesi sonrası ise %84 ve %71 olarak bulunmuştur. 400 nM erastinle yapılan kombinasyon tedavisinde hücre canlılığı sırasıyla %67 ve %45'e düşmüştür. Fer-1 ön muamelesi sonrası kombinasyonlarda bu oranlar %89 ve %70; DFOM sonrası ise %82 ve %68 olarak kaydedilmiştir. İstatistiksel analizlerde $p<0,05$ anlamlı kabul edilmiştir.

Sonuç: RG7388'in, tek başına uygulamasına kıyasla, erastin ile kombinasyonu hücre ölümünü belirgin ve anlamlı şekilde artırmaktadır. Fer-1 ve DFOM ile yapılan ön muameleler, tek başına RG7388'in indüklediği hücre ölümünü anlamlı şekilde engellememiştir. Ancak RG7388 ve erastin kombinasyonunda, ferroptoz inhibitörleriyle ön muamele, hücre ölümünde anlamlı bir azalma sağlamıştır. Bu bulgular, RG7388'in erastin ile birlikte kullanıldığında güçlü bir ferroptotik etki oluşturduğunu ve bu kombinasyonun nöroblastom tedavisinde potansiyel bir strateji olabileceğini düşündürmektedir.

Anahtar Kelimler: Nöroblastom, RG7388, idasanutlin, erastin, ferroptoz

Anadolu Üniversitesi BGT-2023-2343 kodlu proje kapsamında desteklenmiştir.

Oral Presentation – 68

Prostat Kanserinde Mitofaji İnhibisyonunun Radyosensitizan Bir Yaklaşım Olarak Kullanımı

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Giriş ve Amaç: Prostat kanseri, erkeklerde en sık görülen malignitelerden biri olup, kansere bağlı mortalitenin önde gelen nedenlerindendir. Radyoterapi standart bir tedavi seçeneğidir; ancak radyasyon direnci tedavi başarısını sınırlandırmaktadır. Bu direnç mekanizmalarının aydınlatılması, daha etkili tedavi stratejilerinin geliştirilmesini sağlayabilir. Mitokondriyal dinamikler ve mitofaji, hücrelerin strese verdiği yanıtlarda — özellikle radyasyon kaynaklı hasarlarda — kritik roller üstlenmektedir. Bu çalışmanın amacı, mitofajinin inhibisyonunun prostat kanseri hücrelerinin radyasyona duyarlılığı üzerindeki etkilerini değerlendirmek ve mitofajiyi hedeflemenin terapötik potansiyelini araştırmaktır.
Gereç ve Yöntem: Çalışmada radyasyona dirençli (PC3) ve duyarlı (LNCaP) prostat kanseri hücre hatları kullanılmıştır. Hücrelere iyonize radyasyon ve/veya mdivi-1 uygulanmış; radyosensitivite, klonojenik sağkalım analizi ile değerlendirilmiştir. Ayrıca, hücrelerin migrasyon yetenekleri yara iyileşme deneyi ile test edilmiştir. Mitofaji düzeyleri, floresan mikroskopi, western blot ve ROS tespiti ile analiz edilmiştir. Mdivi-1 için etkili doz ve süre, mtDNA kopya sayısı ve floresan analizler ile optimize edilmiştir.
Bulgular: Mdivi-1, PC3 hücrelerinde doz bağımlı olarak mitokondriyal stres toleransını azaltmış ve radyasyon duyarlılığını anlamlı düzeyde artırmıştır. Kombine uygulama, PC3 hücrelerinde ölümcül doz değerini 19,7 Gy'den 4,3 Gy'ye düşürmüştür. LNCaP hücrelerinde migrasyon anlamlı şekilde azalırken ($p<0,01$), PC3 hücrelerinde göç kapasitesi değişmemiştir. 4 Gy radyasyon uygulamasında ROS düzeylerindeki belirgin artış, oksidatif stresin hücre ölümündeki rolünü işaret etmiştir. Aynı dozda mitofaji oranında gözlemlenen en yüksek düşüş, radyasyona olan duyarlılığın mitofaji ile ilişkili olduğunu düşündürmektedir.
Tartışma: Bu çalışma, mitofajinin prostat kanseri hücrelerinde radyasyon direncinde önemli bir rol oynadığını ortaya koymaktadır. Mitokondriyal dinamiklerin hedeflenmesi, radyoterapi etkinliğini artırmada potansiyel bir strateji sunabilir. Elde edilen veriler, mitofajinin modüle edilmesinin, radyoterapi yanıtını artırmak için kullanılabilecek yenilikçi bir yaklaşım olabileceğini düşündürmektedir. Mdivi-1 gibi mitofaji inhibitörlerinin klinik faydasını değerlendirmek amacıyla ileri çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Mitofaji, Mdivi-1, Prostat Kanseri, Radyasyon Direnci, Radyosensitivite

Oral Presentation – 69

Antiproliferatif and Proapoptotic Effects of Aquilaria agallocha Methanolic Extract on Human Breast Cancer Cell Lines

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Introduction and Aim: Breast cancer is one of the most common malignancies in women and is a major public health problem with high incidence and mortality rates. The limitations of current treatments have increased interest in less toxic and effective alternatives. Aquilaria agallocha, which contains phenolic and flavonoid compounds, is a traditional herb characterised by anticancer activity. In this study, the antiproliferative and proapoptotic effects of A. agallocha methanol extract on breast cancer cells were evaluated.

Materials and Methods: A. agallocha methanol extract was prepared and applied to MCF-7 and MDA-MB-231 cell lines; cytotoxicity analysis was performed by MTT method at concentration ranges of 10-80 µg/ml and 10-50 µg/ml, respectively, and apoptosis and cell cycle analysis was performed by Muse Cell Analyzer.

Results: According to the MTT assay, the IC_{50} values of MCF-7 and MDA-MB-231 cell lines were 48.61 µg/ml and 46.84 µg/ml, respectively, after 24 hours of treatment. Annexin V apoptosis analysis revealed 19.57% and 22.32% early apoptosis and 65.22% and 29.47% late apoptosis after treatment at the IC_{50} dose. According to cell cycle analysis, 9.0% of MCF-7 cells were in G0/G1, 44.8% in S, 26.9% in G2/M phase, while the debris rate was 99.7%. In MDA-MB-231 cells, 57.2% were in G0/G1, 19.3% in S, 20.5% in G2/M phase and the debris rate was 64.6%.

Conclusions: *A. agallocha* extract showed antiproliferative effects and induced different apoptosis responses in both breast cancer cell lines. The predominance of late apoptosis in MCF-7 and early apoptosis in MDA-MB-231 is associated with sensitivity to the timing of apoptosis and rapid apoptotic response, respectively. Cell cycle results supported this difference; accumulation in S phase and intense cell destruction were detected in MCF-7, whereas in MDA-MB-231, arrest was detected in G0/G1 phase. The results suggest that the extract induces subtype-specific responses and shows promise in targeted therapies.

Key words: Aquilaria agallocha; Breast cancer; Apoptosis; Cell cycle; Antiproliferative effect

Oral Presentation – 70

Effects of Dracaena Cinnabari Resin Ethanol and Methanol Extracts on Proliferation and Apoptosis in a Human Breast Cancer Cell Line

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Introduction and Aim: Breast cancer is one of the leading causes of cancer-related deaths in women, and metastasis and therapeutic resistance complicate the treatment process. *Dracaena cinnabari* resin is widely used in traditional medicine for its anti-timor, anti-inflammatory, antimicrobial, and antioxidant properties. This study investigated the effects of ethanol and methanol extracts of *Dracaena cinnabari* resin on apoptosis and cell proliferation in human breast cancer MCF-7 cell lines.

Materials and Methods: In this study, *Dracaena cinnabari* resin was obtained from the Socotra Island of Yemen. Ethanol and methanol extracts were prepared from the resin and applied to the human breast cancer cell line (MCF-7) as well as the normal kidney cell line (HEK-293). MCF-7 cells were treated with extract concentrations ranging from 10 to 200 µg/ml, and cell proliferation was assessed using the MTT assay. Apoptosis levels were analyzed using the CytoFLEX flow cytometry system.

Results: In the MCF-7 cell line, the effects of Dracaena cinnabari ethanol and methanol extracts on cell viability were evaluated following 24 and 48 hours of treatment. IC_{50} values were calculated using GraphPad Prism software. At the end of 48 hours, the IC_{50} values for the ethanol and methanol extracts were determined to be 58.69 µg/ml and 65.19 µg/ml, respectively. These IC_{50} concentrations, identified in MCF-7 cells, were subsequently applied to the HEK-293 cell line, where cell viability rates at 48 hours were found to be 65.75% and 45.59%, respectively. In apoptosis analysis, treatment of MCF-7 cells with the IC_{50} doses of the ethanol extract induced 0.18% early apoptosis and 96.93% late apoptosis, while the methanol extract induced 0.07% early apoptosis and 99.70% late apoptosis.

Conclusions: This study demonstrated that ethanol and methanol extracts of Dracaena cinnabari resin exhibit significant cytotoxic and pro-apoptotic effects on MCF-7 breast cancer cells. These findings support the potential of the extracts as anticancer agents and highlight the need for further investigations to explore their therapeutic applications.

Key words: Breast cancer, Proliferation, Apoptosis, *Dracaena cinnabari*

Oral Presentation – 71

Orchis Spitzelii-Mediated Synthesized Gold Nanoparticles and Their Size-Dependent Anticancer Activity in Lung Cancer

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Introduction and Aim: Non-small cell lung cancer (NSCLC) is the most common and deadly malignancy in all populations. Nanotechnology-based cancer therapeutics have been created to increase specificity in cancer treatment. Biosynthesised gold nanoparticles (AuNPs), one of the new therapeutic agents, have attracted the most attention among metallic nanoparticles due to their stability, low chemical reactivity, ability to interact with cells and generally easy localisation in dynamic structures such as tissue. Our study, the effect of size difference of AuNPs biosynthesised via Orchis Spitzelii (Salep) on the epithelial-mesenchymal transition (EMT) process was evaluated.

Materials and Methods: AuNPs biosynthesized via Orchis Spitzelii in magnetic stirrer with different sizes were characterized by UV-Vis, XRD, FT-IR, DLS, Zeta potential, TEM and FESEM-EDX methods. Cytotoxic effect against NCI-H441 and HUVEC cell lines treated with AuNPs for 24 hours and at different concentrations was evaluated by MTT assay. The effect of AuNPs on the EMT process was evaluated by qRT-PCR (CD36, PPARγ, VEGFR2, TIMP2, MMP-2) and Western Blot (MMP-2) methods.

Results: As a result of the cell viability test of AuNPs, it was determined that their cytotoxicity increased in both cancer and healthy cells as their size decreased. Biosynthesised AuNPs were observed to have higher biocompatibility against healthy cells compared to cancer cells. As a result of qRT-PCR, it was concluded that AuNPs upregulated the expression of PPARγ, CD36 and TIMP-2 genes and downregulated the expression of MMP2 and VEGFR2 genes associated with angiogenesis and EMT process. Western blot study also showed that MMP-2 protein level was suppressed in parallel with qRT-PCR study.

Conclusion: Our data, together with the low toxicity profile of AuNPs, suggest that these nanoparticles may serve as potential therapeutic agents to inhibit metastasis.

Keywords: Green synthesis, Gold nanoparticle, Matrix Metalloproteinase 2, Non-small cell lung cancer, Orchis Spitzelii (Salep), Size Effect

References:

Tian, L., Lu, L., Qiao, Y., Ravi, S., Salatan, F., & Melancon, M. P. (2016). Stimuli-responsive gold nanoparticles for cancer diagnosis and therapy. *Journal of functional biomaterials,* 7(3), 19.

Mao, W., Kim, H. S., Son, Y. J., Kim, S. R., & Yoo, H. S. (2018). Doxorubicin encapsulated clicked gold nanoparticle clusters exhibiting tumor-specific disassembly for enhanced tumor localization and computerized tomographic imaging. *Journal of Controlled Release*, 269, 52-62.

Hosny, M., Fawzy, M., El-Badry, Y. A., Hussein, E. E. ve Eltaweil, A. S. (2022). Plant assisted synthesis of gold nanoparticles for photocatalytic, anticancer, and antioxidant applications. *Journal of Saudi Chemical Society*, 26(2), 101419.

Enea, M., Pereira, E., Costa, J., Soares, M. E., da Silva, D. D., de Lourdes Bastos, M., & Carmo, H. F. (2021). Cellular uptake and toxicity of gold nanoparticles on two distinct hepatic cell models. *Toxicology in Vitro*, 70, 105046.

Poster Presentation – 01

Urinary CRK Concentration Analysis for the Prediction of Recurrence in Non Muscle Invasive Bladder

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Introduction and Aim: Bladder cancer (BC) is the 9th-most lethal malignancy in men [1]. Minimally invasive methods are being developed for the diagnosis and follow-up of BC. In this context, urine biomarkers are of significant value, as a non-invasive alternatives [2–4]. The proto-oncogene product CRK, which functions as an adaptor protein, influences cell adhesion and migration. We hypothesized that urinary CRK levels might be associated not only with BC diagnosis but also with patient survival, recurrence, and metastasis. Here we aimed to analyze the prognostic potential of the urinary CRK concentration at the time of diagnosis among recurrent and non-recurrent non muscle invasive bladder cancer (NMIBC) patients.

Materials and Methods: Urine samples were collected from 38 patients diagnosed with NMIBC as well as from 30 healthy controls. The median follow-up duration was 48 months. Urine CRK and Creatinine concentrations were measured using ELISA, and the relationships between urinary concentrations and clinical outcomes were analyzed using SPSS.

Results: The mean urinary CRK/Cr level in bladder cancer patients was significantly higher than in healthy controls ($p<0.0001$). When analyzed based on recurrence, CRK/Cr level in recurrent patients were higher than those in both healthy controls and non-recurrent patients ($p<0.0001$ and $p = 0.018$, respectively). However, there was no significant difference between the urinary CRK levels of healthy controls and non-recurrent patients ($p > 0.05$). The same trend was observed in different risk groups.

Discussion: CRK/Cr levels of bladder cancer patients were higher than controls. However, there was no significant difference between non-recurrent patients and healthy controls, suggesting that CRK is a promising biomarker for bladder cancer recurrence. Incorporating CRK into biomarker studies with larger patient groups may help identifying those at risk of relapse.

Key words: Biomarker; Bladder Cancer; Follow-up; Non-invasive; Recurrence; Survival

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68(6):394-424. doi:10.3322/caac.21492

2. Armstrong DA, Green BB, Seigne JD, Schned AR, Marsit CJ. MicroRNA molecular profiling from matched tumor and bio-fluids in bladder cancer. *Mol Cancer*. 2015;14(1):194. doi:10.1186/s12943-015-0466-2

3. Sapre N, Macintyre G, Clarkson M, et al. A urinary microRNA signature can predict the presence of bladder urothelial carcinoma in patients undergoing surveillance. *Br J Cancer*. 2016;114(4):454-462. doi:10.1038/bjc.2015.472

4. Ratert N, Meyer HA, Jung M, et al. MiRNA profiling identifies candidate mirnas for bladder cancer diagnosis and clinical outcome. *J Mol Diagnostics*. 2013;15(5):695-705. doi:10.1016/j.jmoldx.2013.05.008

Poster Presentation – 02

Dual Inhibition of PFKFB3 and ODC1 Exhibits Enhanced Antiproliferative Effect on Pancreatic Cancer Cells

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Introduction: Pancreatic adenocarcinoma is one of the deadliest cancers, and incidence is on the rise. Activating mutations in the *KRAS* gene confers an aggressive metabolic phenotype in pancreatic adenocarcinoma, which may present therapeutic vulnerabilities. Hyperactive KRAS stimulates glycolysis that is associated with malignant properties, including chemoresistance, suggesting that targeting glycolysis may be a viable therapeutic strategy. Targeting glycolysis, particularly through the glycolytic regulator PFKFB3, offers a promising therapeutic strategy. The glycolytic regulator 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase-3 (PFKFB3) has been shown to be an attractive target to curb aberrant glycolytic activity in tumor cells. In this study, we set out to study the effect of dual targeting of PFKFB3 and ornithine decarboxylase 1 (ODC1), the rate-limiting enzyme of polyamine synthesis pathway.

Material and Methods: In this study, we explored the dual targeting of PFKFB3 and ornithine decarboxylase 1 (ODC1), the key enzyme in the polyamine synthesis pathway, in pancreatic adenocarcinoma cell lines PANC-1 and MIA PaCa-2. We utilized specific siRNA molecules to silence PFKFB3 and ODC1 expressions and employed clinical-grade inhibitors KAN0438757 and DFMO to block their enzymatic activities. Forty-eight hours after treatment, cell viability was assessed using sulforhodamine B and crystal violet assays. Clonogenic assays were also performed to evaluate colony formation after combined treatment.

Results and Discussions: Dual silencing of PFKFB3 and ODC1 significantly suppressed cell proliferation compared to individual targeting. Additionally, subtoxic doses of KAN0438757 enhanced the sensitivity of pancreatic adenocarcinoma cells to DFMO treatment, further reducing clonogenic potential. These findings indicate that PFKFB3 and ODC1 may cooperate to sustain the proliferative and clonogenic abilities of pancreatic adenocarcinoma cells.

Conclusion: Dual inhibition of glycolysis and polyamine synthesis via PFKFB3 and ODC1 targeting represents a potential therapeutic strategy to manage pancreatic adenocarcinoma more effectively.

Poster Presentation – 03

Characterization of a Novel Intronic RNA in Breast Cancer and Its Possible Interactions with microRNAs

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Introduction and Aim: Breast cancer is the second leading cause of cancer-related mortality in women, largely due to its heterogeneity and challenges in treatment resistance. Despite the discovery of new long non- coding RNA (lncRNA) types and their contributions in cancer by the advancements in sequencing, intronic regions remain overlooked and their function is unknown in cancer. Our aim is to investigate a previously unannotated intronic RNA and its potential interactions with microRNAs (miRNAs) in breast cancer.

Materials and Methods: We performed paired-end RNA sequencing on three different breast cell lines: triple-negative breast cancer (HCC1143), ER+/PR+/HER2+ breast cancer (BT474), and a healthy cell line (MCF10A) to investigate unannotated RNAs derived from introns using our in-house developed Nextflow-based pipeline. By the integration of Cap Analysis of Gene Expression (CAGE) and polyadenylation signals (PAS), the ends of intronic transcripts were defined. 5’ and 3’ boundaries of a differentially expressed RNA candidate were validated via rapid amplification of cDNA ends (RACE). The expression profile of the candidate was analyzed across cell lines representing 40 cancer types from the Cancer Cell Line Encyclopedia (CCLE), with miRNA interactions predicted using miRBase.

Results: Our RNA-seq data identified a novel intronic RNA that is upregulated in cancer cell lines compared to the healthy control. RACE analysis confirmed its precise boundaries, establishing it as a distinct transcript. The UCSC Alt Events Track revealed the presence of an alternative promoter near its 5′ end. Pan-cancer analysis showed its expression across multiple cancer types, while *in silico* predictions identified potential interactions with several miRNA precursors, including hsa-miR-1273h.

Discussion: Our study demonstrates the existence of a conserved intronic RNA with possible interactions with miRNA precursors. These findings suggest its potential functionality across malignancies possibly by interacting with miRNAs. These findings expand the ncRNA landscape and highlight intronic transcripts as promising candidates in breast cancer progression.

Poster Presentation – 04

Investigating the effects of long non-coding RNAs in triple negative breast cancer pathogenesis

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Introduction and Aim: Breast cancer is the most common cancer in women, with Triple-Negative Breast Cancer (TNBC) accounting for 10-20% of cases. TNBC is aggressive and lacks estrogen (ER), progesterone (PR), and HER2 receptors, making hormone treatments ineffective. Over the last decade, long non-coding RNAs (lncRNAs) have gained interest due to their regulatory role in gene expression. This project investigates the effects of two dysregulated lncRNAs in the TNBC cell line HCC1143 compared to the healthy MCF10A cell line. Understanding their role in TNBC could lead to novel therapies, improving treatment and patient survival.

Materials and Methods: Two upregulated lncRNA candidates in HCC1143 cell line were selected based on TNBC-associated SNPs and their corresponding protein-coding genes' functions in TNBC. The miRBase database was used to assess potential interactions between these lncRNAs and miRNAs. RT-qPCR experiments validated the expression levels of the selected candidates in MCF10A and HCC1143 cell lines.

Results: RNA-seq analysis revealed a Log2 fold change of 4.56 for an antisense lncRNA and 3.85 for a divergent transcript in HCC1143 cells compared to MCF10A ($P < 0.05$). MiRBase data indicated a potential interaction between the antisense lncRNA and the hsa-miR-6847 precursor miRNA, while the divergent transcript was linked to seven precursor miRNAs, including hsa-miR-619, which is associated with cancer pathogenesis. A study has shown that the protein-coding gene associated with the antisense lncRNA likely contributes to TNBC's mutation profile. Similarly, the divergent transcript's protein-coding gene functions as a novel oncogene and potential therapeutic target in TNBC according to literature. qPCR analysis showed a Log2 fold change of 4.75 for the antisense lncRNA and 4.12 for the divergent transcript compared to MCF10A.

Discussion: Our results suggest that these two lncRNAs may contribute to TNBC pathogenesis. Further research using Antisense LNA GapmeRs for silencing is required to examine their effects on cancer-like phenotypes in HCC1143 cells.

Poster Presentation – 05

Investigating the role of fucosyltransferase genes on cancer stem cell potential-associated phenotypes in head and neck squamous cell carcinoma

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Introduction and Aim: Despite advances in diagnosis/treatment methods, there has been no remarkable increase in overall survival of HNSCC patients in recent years due to diagnosis of disease in later stages and frequent recurrence of primary lesions. Post-translational modifications regulate numerous cellular processes. Recent studies have shown that fucosylation, one of the post-translational modifications, is significantly associated with cancer pathogenesis. So far, 13 fucosyltransferase synthesis genes have been identified in the human genome, including FUT1-11 and Protein O fucosyltransferase 1-2.

Materials and Methods: In this study, firstly we detected the expression changes of FUTs in tumor and normal tissue sample pairs taken after surgery from patients diagnosed with head and neck cancer using real-time PCR technique at mRNA level. Then, we evaluated the expression of FUT7 and FUT9 in head and neck cancer tumor tissues compared to normal tissues, at protein level in tumor-normal tissue pairs by western blot analysis. In addition, we investigated the expression changes of FUT7 and FUT9 in head and neck cancer and normal oral fibroblast cells at mRNA and protein levels. Then, we analyzed the role of FUT7 and FUT9 on cancer stem cell potential in tumor cell-derived spheroids and adherent cells.

Results: We detected that FUT7 and FUT9 expressions were increased at mRNA and protein levels in tissue samples taken from HNSCC patients. Also we confirmed that FUT7 and FUT9 had increased expression in head and neck cancer cells. We then found that FUT7 and FUT9 were highly expressed in tumor spheroids derived from head and neck cancer cells compared to adherent cells.

Discussion: These results suggest FUT7 and FUT9 expression as a potential prognostic marker for patients with HNSCC and their increased expression is closely associated with cancer stem cell potential.

Poster Presentation – 06

Identification of the 3' UTR mutations of the *IL7R* gene in lung cancer, breast cancer, and melanoma

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Introduction and Aim: Our previous study (Congur et al. 2023) identified *IL7R* as one of the commonly mutated genes that cause metastases from skin, breast, and lung tissues, which lead to the progression of leptomeningeal carcinomatosis. However, its role in solid cancers is not well studied. Moreover, there isn't much research focusing on miRNAs' effect on *IL7R* transcript in the above-mentioned solid tumors in the literature. This study aims to identify the impacts of the *IL7R* 3'UTR mutations observed in lung, breast, and skin cancers by assessing the altered miRNA binding sites using *in silico* tools.

Materials and Methods: In this study, the 3'UTR mutations of the *IL7R* gene were exported from the Ensembl Genome Database on 09.12.2024. The miRNAs interacting with the 3'UTR of the canonical *IL7R* transcript (ENST00000303115.8) were analyzed by using miRDB (MicroRNA Target Prediction Database), miRWalk v. 3, and mirPath v.3 DIANA Tool. The common miRNAs were identified, and seed sequences were mapped to the mutated 3'UTR of *IL7R*.

Results: 1577 3'UTR mutations were detected via Ensembl Genome Database. Moreover, 142 miRNAs binding to the 3'UTR by miRDB and 635 miRNAs by miRWalk were identified. 25 miRNAs were common between the miRDB and the miRWalk data. These common miRNAs were further investigated with mirPath v.3 DIANA Tool to check their binding to the *IL7R* transcript. This analysis revealed 8 miRNAs: hsa-miR-4659b-3p, hsa-miR-4659a-3p, hsa-miR-6740-3p, hsa-miR-6133, hsa-miR-4510, hsa-miR-6129, hsa-miR-670-3p, hsa-miR-511-5p.

Discussion: Though these miRNAs lack prior association with breast, lung, or skin cancers in the literature, our novel *in silico* findings suggest their potential involvement, highlighting the need for further experimental validation *in vitro.* Further analysis will be performed to reveal the network of genes with which these miRNAs interact. Moreover, *in vitro* studies are required to identify the impact of the candidate 8 miRNAs in lung, breast, and skin cancers.

Key words: miRNA, lung cancer, breast cancer, melanoma, *IL7R*

Reference:

1. Congur I, Koni E, Onat OE, Tokcaer Keskin Z. Meta-analysis of commonly mutated genes in leptomeningeal carcinomatosis. PeerJ. 2023 Apr 19;11:e15250. doi: 10.7717/peerj.15250. PMID: 37096065; PMCID: PMC10122459.

Poster Presentation – 07

Evaluating BD1008 as a Promising Therapeutic Candidate in Glioblastoma Treatment

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Glioblastoma (GBM) is an aggressive and fatal brain cancer in adults, characterized by rapid progression and poor prognosis. Despite ongoing advancements, current treatment options remain limited and challenging. Temozolomide (TMZ), an alkylating chemotherapeutic agent, is the primary treatment for GBM; however, its efficacy is restricted to approximately 50% of patients, depending on the methylation status of the O6-methylguanine-DNA methyltransferase (*MGMT*) gene. This limitation underscores the urgent need to explore novel therapeutic agents and alternative treatment strategies to improve patient outcomes. Recent bioinformatics analyses have identified the Sigma-1 receptor as a potential therapeutic target in GBM. This receptor is primarily located in the mitochondria-associated membrane (MAM) region of the endoplasmic reticulum (ER) and functions as both a receptor and a chaperone. Inhibiting Sigma-1 receptor is predicted to induce secondary messengers, ER stress and apoptotic caspase cascade. BD1008, a selective Sigma-1 receptor antagonist, was evaluated for its therapeutic potential in U87 and LN18 GBM cell lines. MTT cell viability assays revealed that BD1008, when administered alone, induced approximately 50% cell death in both GBM cell lines. Additionally, its combination with TMZ did not enhance cytotoxicity beyond the effect of BD1008 alone, suggesting a distinct mechanism of action. Colony formation assays further demonstrated that BD1008 significantly impaired the ability of GBM cells to form colonies, indicating its potential to disrupt long-term cancer cell proliferation. Furthermore, fluorescence-based assessments of mitochondrial membrane integrity and cell survival confirmed that BD1008 induces cellular stress, leading to apoptosis. In 3D cell models, such as hanging drop assay, BD1008 inhibited anchorage-independent tumor growth, a key feature of aggressive GBM cells. Finally, Annexin V-PI staining assays confirmed that BD1008 treatment led to apoptotic cell death. These findings highlight BD1008 as a promising candidate for further investigation in GBM therapy.

Poster Presentation – 08

Unraveling the Role of TAp73β in Hepatocellular Carcinoma by Driving Metastasis, Angiogenesis, and Sorafenib Resistance in the Zebrafish Xenograft Model

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Introduction and Aim: Hepatocellular carcinoma (HCC) is the most common liver cancer and ranks third among cancer-related causes of death. Sorafenib is a receptor tyrosine kinase inhibitor that is used for the treatment of advanced HCC. However, resistance to Sorafenib emerges within a very short period. To develop more efficient therapeutic approaches, the underlying molecular mechanisms of Sorafenib resistance need to be elucidated. This study aims to investigate the molecular mechanisms of TAp73β mediates metastasis, angiogenesis and Sorafenib resistance in HCC using RNA sequencing analysis.

Materials and Methods: To test the effect of TAp73β expression on angiogenesis, metastasis and Sorafenib resistance in HCC cell lines, 2 days post-fertilization (dpf) Flia1:GFP zebrafish larvae were used. RNA was isolated from the zebrafish xenograft, and RNA sequencing was performed. Zebrafish-derived RNA-Seq reads were filtered using Disambiguate v5.03-9 software to prevent misalignments originating from the xenograft host. Differential gene/transcript expression between groups was obtained using DESeq2 v1.42.0 software. From the list of significantly altered genes, target genes associated with metastasis, angiogenesis, and Sorafenib resistance were identified and validated using qPCR.

Results: Our results showed that TAp73β promotes metastasis, angiogenesis, and Sorafenib resistance in Hep3B, an HCC cell line. Furthermore, RNA sequencing analysis was conducted by separating zebrafish and human genes, focusing on human-specific genes. RNA-Seq analysis revealed candidate genes involved in TAp73β-mediated metastasis, angiogenesis, and Sorafenib resistance in HCC, and their expressions were confirmed at the transcript level.

Discussion: Our study demonstrated that TAp73β induces angiogenesis, metastasis, and Sorafenib resistance in HCC cell lines in the zebrafish xenograft model. Moreover, overexpression of TAp73β led to an increase in the expression of genes associated with an aggressive cancer phenotype. In conclusion, our results suggest that TAp73β enhances metastasis and angiogenesis through extensive gene interactions in the zebrafish xenograft model.

Key words: Hepatocellular carcinoma, p73, zebrafish xenograft model, sorafenib resistance, RNA-sequencing

This study was supported by the Scientific and Technological Research Council of Türkiye (TUBITAK, grant number 222z254).

Poster Presentation – 09

Investigation of the Differential Effects of L-Glutamine Starvation on Lipid Droplet Formation and Migration Capacity of Colorectal Cancer Cells SW480 and SW620

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Introduction and Aim: Glutamine is a non-essential amino acid that fuels the TCA cycle to support cell proliferation. While crucial for cancer metabolism, its distinct effects on metastatic vs primary colorectal cancer (CRC) cells remain unclear. SW480 and SW620 are paired primary and metastatic CRC cell lines commonly used for comparison studies. Our previous work showed that glutamine starvation boosts lipid synthesis/uptake in both cell lines, accompanied by enhanced SW620 cell migration.[1] Since glucose and glutamine usage are reciprocally regulated[2], high levels of one may reduce the usage of the other. This study explores how glutamine starvation affects lipid droplet formation and migration in glucose- or galactose-fed SW480 and SW620 cells.

Materials and Methods: Nile red staining was applied to assess lipid droplet formation in response to glutamine starvation in glucose- or galactose-fed cells. Colony formation and wound healing assays were applied to assess proliferation and migratory capacities, respectively, of glucose- or galactose-fed cells upon glutamine starvation.

Results: The percentages of lipid droplets containing cells increased in both cells upon glutamine starvation in both glucose and galactose-fed cells. Upon FBS withdrawal a drastic decrease in lipid droplet content was observed in SW480 cells, while high lipid droplet content was persistent in SW620 cells. Both cell lines preserve their proliferative and migratory capacities when glutamine withdrawn from glucose-fed cells, while galactose-fed cells were more sensitive to glutamine starvation. Withdrawal of FBS was able to suppress the migration and proliferation of both cell lines effect being more prominent in SW620 cells.

Discussion: Our results indicate that both cell lines are more reliant of glutamine when they are fed with galactose instead of glucose. SW620 cells exhibit greater metabolic plasticity, showing higher resistance to withdrawal of both FBS and glutamine. Differences in lipid content suggest alternative metabolic adaptations between used cell lines.

References:

1. Güleç Taşkıran, A. E. *et al.* Glutamine withdrawal leads to the preferential activation of lipid metabolism in metastatic colorectal cancer. *Transl. Oncol.* 48, 102078 (2024).
2. Ronald Zielke, H., Ozand, P. T., Tyson Tildon, J., Sevdalian, D. A. & Cornblath, M. Reciprocal regulation of glucose and glutamine utilization by cultured human diploid fibroblasts. *J. Cell. Physiol.* 95, 41–48 (1978).

Poster Presentation – 10

Impact of Glutamine Utilization Through Tricarboxylic Acid Cycle on Lipid Metabolism in SW480 and SW620 Cells

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Introduction and Aim: SW480 and SW620 cells are matched primary and metastatic colorectal cancer (CRC) cells relying on oxidative metabolism. L-glutamine robustly contributes to the cellular energetics of cancer cells through its involvement in the Tricarboxylic Acid Cycle. Previous studies suggested that glutamine starvation leads to an increase in fatty acid synthesis and lipid droplet formation. However, how glutamine starvation contributes to lipid synthesis/uptake is unclear. This study aims to investigate the effects of glutamine starvation and CB-839, a glutaminase inhibitor, comparatively to understand the mechanisms leading to enhanced lipid droplets in SW480 and SW620 cells.

Materials and Methods: SW480 and SW620 cells were either incubated in a medium that does not contain glutamine or treated with 1μM CB-839. Nile red staining was conducted to assess lipid droplet formation, a colony formation assay was applied to assess proliferation, and a wound healing assay was carried out to evaluate migration capacity.

Results: Both cell lines exhibit elevated levels of lipid droplets in response to both glutamine starvation and CB-839 treatment, the effects of CB-839 being less pronounced in SW620 cells. FBS withdrawal limited the lipid droplet formation in both cell lines, the effect is more prominent in SW620 cells. Both cell lines could tolerate glutamine starvation and CB-839 treatment, as indicated by the similar colony formation capacity in all conditions. Scratch assay revealed that FBS availability was the main factor influencing cell migration in both lines, while CB-839 and glutamine levels had minimal impact.

Discussion: Results showed that the entrance of glutamine to the TCA cycle is the major contributor to the increased lipid droplets in SW480 cells, while cellular uptake is the major contributor for SW620 cells. Due to their metabolic plasticity, both cell lines can tolerate CB-389 treatment and glutamine starvation in terms of proliferation and migration.

Key words: Glutamine metabolism, lipid droplets, colorectal cancer, CB-839, SW480, SW620

References:

1. Güleç Taşkıran AE, Karaoğlu DA, Eylem CC, Ermiş Ç, Güderer İ, Nemutlu E, Demirkol Canlı S, Banerjee S. Glutamine withdrawal leads to the preferential activation of lipid metabolism in metastatic colorectal cancer. Transl Oncol. 2024 Oct; 48:102078. doi: 10.1016/j.tranon.2024.102078. Epub 2024 Aug 7. PMID: 39111172; PMCID: PMC11362781.

Poster Presentation – 11

Investigation of the Effects of ZRF1 Protein on Neutrophil Chemotaxis and Polarization *via* Paracrine Signaling in Breast Cancer

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Introduction and Aim: The tumor microenvironment plays a pivotal role in breast cancer metastasis, with tumor-associated neutrophils (TANs) emerging as key contributors. However, the mechanisms driving their functional plasticity remain unclear. S100A9, a critical mediator of inflammation and metastasis, is implicated in TAN-driven tumor progression. ZRF1 (Zuotin-related factor 1), a chromatin- associated protein, regulates S100A9 in breast cancer cells, but its role in neutrophil polarization *via* paracrine signaling is largely unexplored. This study aims to investigate neutrophil adhesion, transendothelial migration, and TAN1/2 gene regulation in the context of ZRF1 deficiency.
Materials and Methods: ZRF1 was stably silenced in the triple-negative breast cancer cell line MDA-MB-231. S100A9 expression was assessed by qRT-PCR, western blot, and ELISA. Conditioned media (CM) from control and ZRF1-knockdown cells were used to treat HL-60-derived neutrophil-like cells. Neutrophil adhesion to HUVECs, TAN1/TAN2 marker expression, and TNFα and IL-8 secretion were evaluated. Transendothelial migration through HUVECs was analyzed *via* xCELLigence and transwell assays.
Results: ZRF1 depletion modulated S100A9 expression depending on serum conditions (10% vs. 0.2% FBS). CM from ZRF1-deficient cells downregulated TAN1 (anti-tumor) markers, while TAN2 (pro-tumor) markers remained unchanged. IL-8 levels were unaffected by short-term CM priming but showed increased internalization with prolonged exposure; TNFα levels were unchanged. ZRF1 knockdown had a subtle yet significant impact on neutrophil adhesion and transendothelial migration. CM priming reduced migration in shZRF1 cells, whereas no priming produced the opposite effect.
Discussion: These findings uncover a novel ZRF1–S100A9–neutrophil axis in breast cancer. ZRF1 shows context-dependent regulation of S100A9 and selectively affects TAN1-related genes. Its effects on neutrophil migration vary with priming conditions. Further studies are needed to determine if ZRF1- driven S100A9 expression alone dictates TAN polarization.
Key words: Breast cancer, ZRF1, tumor-associated neutrophils (TAN), tumor microenvironment (TME).

Poster Presentation – 12

Determination of the Effect of Nutrient Limitation on P-Glyocoprotein Expression and on Pathways Controlling P-gp Expression: Possible Chemosensitization via Verapamil Treatment

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Introduction and Aim: Limited nutrients in the tumor microenvironment regulate cancer cell metabolism. Our previous studies showed that nutrient-limited T84 colorectal cancer (CRC) cells exhibit increased autophagy, enlarged perinuclear lysosomes, and enhanced lysosomal drug accumulation, leading to reduced chemosensitivity. [1] These cells also upregulate MDR1 mRNA, encoding P-glycoprotein (P-gp), a key multidrug resistance protein.[1] While P-gp is known to export drugs at the plasma membrane, it can also localize to organelles like lysosomes and mitochondria. This study investigates the role of P-gp in decreased chemosensitivity of T84 cells under nutrient limited conditions as well as possible signaling pathways that cause an increase in P-gp levels under nutrient-limited conditions.

Materials and Methods: Changes in ERK phosphorylation, HIF-1α protein level expression was evaluated with western blot since these are the pathways that are known to be involved in P-gp regulation and are affected in response to starvation. In addition, the effects of P-gp inhibitor verapamil treatment along with 5-Fluorucil (5-FU) were evaluated with colony formation assay to assess chemosensitivity of T84 cells.

Results: Nutrient limitation leads to increased HIF-1α expression as well as ERK phosphorylation which may be the possible regulators of enhanced P-gp expression. Verapamil treatment does not lead a dramatic change in the expression of P-gp protein, yet verapamil treatment along with the 5-FU treatment decreased the colony formation capacity of both nutrient rich and limited cells effect being more prominent in nutrient limited cells.

Discussion: These results indicated ERK and HIF-1α as possible regulators of enhanced P-gp expression in nutrient limited T84 cells. Furthermore, proliferative capacity of verapamil and 5-FU treated cells decreased probably due to inhibition of P- gp rather than an effect on expression.

Key words: Colorectal Cancer, Nutrient Limitation, P-Glycoprotein

Poster Presentation – 13

Effects of miR-155-5p on migration and autophagy in lung cancer cells

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Introduction and Aim: Lung cancer is one of the most common causes of cancer-related mortality worldwide. Hsa-miR-155-5p is an oncogenic microRNA that exhibits tumor-promoting effects in various cancer types and is overexpressed in lung cancer, where it is associated with poor prognosis. This study examined the effects of miR-155-5p on autophagy and migration as well as its relationship with p53.

Materials and Methods: Autophagy was assessed by fluorescent labeling of autophagosomes, and migration was analyzed using a Real-Time Cell Analyzer (RTCA-Xcelligence). The mRNA expression levels of key molecules, including p53, SIRT1, RHEB, Snail, and vimentin, were evaluated using PCR analysis.

Results: After the A549 cells transfected with hsa-miR-155-5p (50 nM) mimic, p53 and RHEB mRNA expression levels decreased 0.38-fold and 0.4-fold, respectively. However, SIRT1 expression increased 1.6-fold. Fluorescence microscopy revealed a slight increase in autophagosome intensity. After transfection with the miR-155-5p inhibitor (10 nM), p53 and SIRT1 mRNA expression levels increased 1.8-fold and1.4-fold, respectively. RHEB expression decreased to 0.45. Suppression of hsa-miR-155-5p enhances autophagy via p53, RHEB, and SIRT1. Migration analysis showed that hsa-miR-155-5p inhibition reduced migration to 77.8% at 24 h. Snail mRNA expression increased 2.3-fold at 48 h on the other side, vimentin expression decreased by 0.71-fold after mimic transfection. miR-155-5p inhibition reduced migration by decreasing vimentin expression. p53 suppression via siRNA (10 pg/µl) reduced p53 mRNA expression 0.1-fold. Fluorescence microscopy showed that p53 suppression reduced autophagy. Migration studies revealed that increased miR-155-5p expression following p53 suppression enhanced cell migration by 213% at 24 h and 265% at 96 h.

Discussion: The results of this study demonstrated that hsa-miR-155-5p operates in a p53-mediated manner in A549 cells. Furthermore, p53 suppression was found to be inhibit autophagy while enhancing cell migration.

Poster Presentation – 14

Olfactory Receptor OR2A4/7 and its Effects on Epithelial-Mesenchymal Plasticity in Colorectal Cancer

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Introduction: Metastasis is one of the major contributors to the high mortality rates associated with Colorectal Cancer (CRC). Olfactory Receptors (ORs) belong to the G protein-coupled receptor family and play an important role in both the development and progression of cancer. Epithelial-mesenchymal plasticity (EMP) enables cells to transition between various states within the epithelial-mesenchymal landscape, allowing them to acquire hybrid epithelial/mesenchymal phenotypic features.

Aim: This study investigates the potential role of the OR2A4/7 in EMP in CRC cell lines.

Material and Method: Expression Atlas, CCLE, and the Human Protein Atlas were used to analyze the expression levels of OR2A4/7 in different CRC lines. RT-PCR was performed to confirm bioinformatic data. The CRISPR-Cas9 system was used to silence OR2A4/7. The gene inhibition was confirmed at mRNA level. Expression levels of various EMT markers were analyzed by RT-PCR. Biological assays and zebrafish metastasis model were used to determine the functional role of OR2A4/7.

Results: Bioinformatic analyses revealed that OR2A4/7 mRNA expression was higher in the more metastatic CRC cell lines. RT-PCR results were consistent with the bioinformatic analyses. CRISPR studies revealed that OR2A4/7 knockout clones have higher gene expression of some epithelial markers. Preliminary results of zebrafish larval xenograft assay showed that knockout clones had more metastatic potential compared to control groups.

Discussion: This study provides an insight into the presence and the role of OR2A4/7 in EMP development in CRC. Data gathered via bioinformatic analyses, and both in vitro and in vivo analyses underlines that OR2A4/7 may play a significant role in EMP in CRC. Further research may reveal the broader significance of olfactory receptor genes in EMP.

Key words: Colorectal cancer, Olfactory receptors, EMP, CRISPR-Cas9

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Poster Presentation – 15

A Novel Antiproliferative Strategy: Synergistic Inhibition of Cancer Cell Viability via GOT1 Targeting and Cepharanthine

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Introduction and Aim: Targeting metabolic vulnerabilities has emerged as a promising strategy in cancer therapy. Glutamate-Oxaloacetate Transaminase 1 (GOT1), a key enzyme in glutamine metabolism and redox homeostasis, has been implicated in cancer cell proliferation. Although pharmacological inhibition of GOT1 demonstrates antiproliferative activity, its effectiveness may be restricted by compensatory metabolic pathways. This study aimed to screen an FDA-approved anticancer drug library in combination with GOT1 inhibition to identify synergistic compounds with enhanced anticancer efficacy.

Materials and Methods: To inhibit GOT1 activity, a selective small-molecule GOT1 inhibitor (GOT1 inhibitor-1; GOT1i) was used. A combinatorial screen of 1143 FDA-approved anticancer compounds was conducted in HCT116 colorectal cancer cells. Cell viability was assessed using the Sulforhodamine B (SRB) assay, and selected combinations were validated with the CellTiter-Glo assay. Cepharanthine, a natural bisbenzylisoquinoline alkaloid, was identified as a candidate compound exhibiting synergy with GOT1 inhibition. The combination was further evaluated in HCT116, A549, and LLC1 cells using dose-response matrices. The antiproliferative effect of single drugs and their combinations was also assessed in colony formation assays in HCT116 and A549 cells. The combination was tested in the non-tumorigenic lung epithelial cell line BEAS-2B to determine selectivity towards cancer cells.

Results: The combination of cepharanthine with GOT1i exhibited a significantly greater antiproliferative effect on HCT116, A549, and LLC1 cell lines than either inhibitor alone. This combination showed strong synergy based on multiple synergy models, including Bliss independence. In HCT116 and A549 cells, the combination completely abrogated colony formation. The combination exhibited selectivity towards cancer cells, as no significant effect was observed on BEAS-2B cells.

Discussion: These findings indicate that cepharanthine in combination with GOT1i represents a promising combinatorial strategy for targeting cancer cell metabolism. The selective nature of the combination underscores its potential for further preclinical evaluation.

Key words: Lung cancer, GOT1, cepharanthine

Poster Presentation – 16

Exploring ESR1 and Its Transcriptional Network in Luminal Breast Cancer

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Introduction and Aim: Breast cancer is a heterogeneous disease, with ESR1 serving as a crucial biomarker, especially in the luminal subtype. This study aims to identify transcription factors (TFs) associated with ESR1 and investigate their impact on luminal breast cancer.

Materials and Methods: Three open-source datasets were used to compare gene expression between normal (MCF10A, MCF12A) and cancerous (MCF7, T47D) cell lines. DGE analysis was performed using DeSeq2 (p-value < 0.05 and fold-change > 2). This analysis revealed 1,958 upregulated and 1,612 downregulated genes. ESR1 knockdown was further analyzed in two datasets (MCF7 and T47D), identifying 300 upregulated and 264 downregulated genes in MCF7, and 427 upregulated and 866 downregulated genes in T47D. Knockdown was confirmed in both datasets. GSEA was conducted to examine the impact of ESR1 on biological pathways, and survival analysis was performed on top candidate genes.

Results: 102 downregulated and 84 upregulated ESR1-related genes were identified. Intersecting the initial dataset with the knockdown datasets revealed 95 cancer-related genes associated with ESR1. STRING database analysis confirmed ESR1's role as a hub gene with multiple interactions. Among the 95 genes, 9 TFs were identified through the Human Protein Atlas. GSEA highlighted the impact of ESR1 on steroid hormone pathways. Additionally, transcription factor interactions with ESR1 were analyzed using TCGA data. Genes upregulated or downregulated in the luminal subtype and showing no significant changes in other subtypes were prioritized. Decreased *MYB* expression improved survival in the luminal subtype, while increased *MSX2* expression in patients receiving endocrine treatment significantly impacted survival.

Discussion: TFs such as MSX2 and MYB are predicted to play significant roles in ESR1-mediated luminal breast cancer development. While MYB is associated with ESR1 binding, the relationship between MSX2 and ESR1 is novel. Functional studies on MSX2 may offer valuable insights into ESR1's role in breast cancer.

Key words: Bioinformatics, ESR1, Breast cancer, TFs.

Poster Presentation – 17

Effects of Dual Targeting of Malic Enzyme and NRF2 on Cell Viability and Redox Balance in A549 Cells

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Introduction and Aim: Malic enzyme (ME) and nuclear factor erythroid 2-related factor 2 (NRF2) are critical regulators of cellular metabolism and oxidative stress response. Dysregulation of these pathways contributes to cancer cell survival and therapy resistance. This study aimed to investigate the effects of simultaneous targeting of ME and NRF2 on cell viability and redox balance in A549 human lung adenocarcinoma cells.

Materials and Methods: A549 cells were transfected with ME- and NRF2-specific small interfering RNAs (siRNAs) using Lipofectamine reagent (Invitrogen) according to the manufacturer's protocol. The efficiency of gene silencing was confirmed by Western blot analysis. Cell viability was assessed using the CellTiter-Glo® Luminescent Cell Viability Assay (Promega, G7570). Redox status was evaluated by quantifying intracellular $NADP^+$ and NADPH levels using the NADP/NADPH-Glo™ Assay (Promega, G9081) according to the manufacturer's instructions. Statistical analysis was performed using one-way ANOVA followed by Tukey's post-hoc test to determine significant differences between groups.

Results: Western blot analysis confirmed the successful knockdown of ME and NRF2 expression. Dual targeting of ME and NRF2 significantly reduced cell viability compared to the control siRNA group ($p=0.033$). Moreover, NADPH/$NADP^+$ ratios significantly increased following dual knockdown compared to single knockdowns and the control group ($p<0.001$), indicating a pronounced disruption in redox homeostasis.

Discussion: The findings suggest that combined inhibition of ME and NRF2 disrupts cellular redox balance and significantly decreases the viability of A549 cells. Inhibition of ME alone led to an increase in NADPH/$NADP^+$ ratio, suggesting possible compensatory activation of alternative NADPH-producing pathways. These results highlight the synergistic role of ME and NRF2 in maintaining redox homeostasis and promoting cancer cell survival. Targeting both pathways simultaneously may offer a promising therapeutic strategy for lung cancer.

Key words: Malic enzyme, NRF2, A549, oxidative stress, NADP/NADPH, siRNA

Poster Presentation – 18

Deciphering the Role of Purine Metabolic Enzymes in Ovarian Cancer

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Introduction and Aim: Among all gynecological malignancies, ovarian cancer has the worst prognosis since the cases cannot be diagnosed until the last stage of the disease. The lack of both plausible methods for early diagnosis and the specific symptom of the disease results in %70 cases being diagnosed in the last stage of the disease. High-grade serous ovarian carcinoma (HGSOC) is the most aggressive type of epithelial ovarian cancer. Despite the treatments applied, HGSOC relapses with faster spread, metastasis, and resistance to chemotherapy which inevitably causes an increase in the morbidity and mortality of HGSOC. Due to the uncontrolled rapid growth in cancer cells, cancer cells adapt their metabolic mechanisms to the environment. The fundamental requirement for cell growth is the replenishment of the purine pool. Particularly aggressive cancer types are highly dependent on the de novo purine biosynthesis pathway to rapidly proliferate. Therefore, with our study we are aiming to decipher how the enzymes in the de novo purine biosynthesis pathway affect HGSOC pathology and progression.

Materials and Methods: De novo purine biosynthesis enzymes' expressions will be detected in CAOV3, OVSAHO, and Kuramochi cell lines, which are HGSOC cell lines and have been shown to have different levels of aggressiveness in studies. As an ideal candidate in de novo purine synthesis pathway, PAICS gene will be expressed ectopically in the least expressing HGSOC cell line via the overexpressing lentiviral vector system. After that, proliferation/growth rates, invasion capacities, colony formation, EMT, and cancer stem cell potentials will be revealed in this cell in order to understand whether the overexpression of PAICS gene may cause tumor aggressiveness.

Results: Our in-silico analyses revealed that PAICS expression is significantly elevated in HGSOC cancer cells compared to normal conjugate. Moreover, the increase in PAICS expression in HGSOC tumor samples was detected to be also positively associated with tumor grade and stage both mRNA and protein level. In correlation with in-silico results, we showed that mRNA and protein level PAICS expression was higher in relatively more aggressive HGSOC cell lines in respective order of CAOV3, Kuramochi and OVSAHO.

Conclusion: Overall, according to our in-silico and in-vitro data, PAICS can be ideal candidate biomarker for targeting HGSOC.

Key words: HGSOC, de novo purine biosynthesis, PAICS

Poster Presentation – 19

EZH2 Inhibitor Tazemetostat Effect on Apoptosis and WNT Signaling Pathway in Anaplastic Thyroid Cancer Cells

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Introduction and Aim: Anaplastic thyroid cancer (ATC) has a high mortality rate, with a 90% cancer-specific death rate and a median survival of 4-6 months. EZH2 overexpression is linked to poor prognosis, and while it is overexpressed in ATC, it is not altered in other thyroid cancer types. Wnt signaling is important for thyroid homeostasis and cell proliferation. This study investigates the anti-cancer potential of the EZH2 inhibitor Tazemetostat in ATC cells, particularly its effects on apoptosis and Wnt pathway gene expression.

Materials and Methods: SW-1736 cells were cultured in DMEM and incubated under appropriate conditions. Proliferation and cytotoxicity analyses were assessed using the WST-1 assay, and the IC50 value of Tazemetostat was determined. Apoptosis analysis was performed using Annexin V/PI staining and flow cytometry. For gene expression analyses, total RNA isolation was carried out, and cDNA synthesis was performed. Expression changes of Wnt pathway-related genes were determined by qRT-PCR and analyzed using the $2^{-\Delta\Delta Ct}$ method.

Results: SW-1736 cells were treated with Tazemetostat for 24, 48, and 72 hours. The IC50 doses were 79.98 μM, 33.90 μM, and 46.10 μM, respectively. The effects of Tazemetostat on SW-1736 cells in relation to apoptosis were investigated using an apoptosis assay and flow cytometry. Upon treatment with 34 μM Tazemetostat for 24, 48, and 72 hours, apoptotic cells were observed at rates of 2.6%, 3.36%, and 3%, respectively. The gene expression changes observed in SW-1736 cells following Tazemetostat treatment show significant effects, particularly in the Wnt signaling pathway, proliferation, and invasion processes.

Discussion: Tazemetostat treatment in SW-1736 anaplastic thyroid cancer cells induced apoptosis and altered the Wnt signaling pathway. These results suggest Tazemetostat's potential as a therapeutic for anaplastic thyroid cancer, warranting further in vivo investigation.

Key words: Anaplastic Thyroid Cancer, EZH2, WNT Signaling Pathway, Apoptosis

Poster Presentation – 20

Investigation of Methylation-Related Expression Changes of *GABRB3* Gene in Oral Malignant Lesions.

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Introduction-Purpose: Oral cancer constitutes 2-4% of all cancers and is the most common cancer in the head and neck region after laryngeal cancer. Oral squamous cell carcinoma (OSCC) constitutes more than 90% of all oral cavity carcinomas. While the 5-year survival rate in OSCC is 40%, this rate increases to 95% in early diagnosis. The *GABRB3* gene was identified as a potential epigenetic biomarker candidate in the TUBITAK-SBAG-114S497 project conducted by Demokan et al., and in this study, the differing methylation and expression levels in OSCC patients were examined and its biomarker potential in early diagnosis and prognosis was investigated.

Materials-Methods*:* DNA and RNA were isolated from tissue samples taken from 15 patients diagnosed with OSCC, then the methylation status and gene expression levels of the *GABRB3* gene were evaluated by Quantitative Methylation Specific PCR and Real-Time PCR methods, respectively.

Results: Methylation was detected in the promoter region of the GABRB3 gene in 60% of tumor samples from OSCC patients. When expression levels were evaluated, loss of expression of the *GABRB3* gene was detected in 46.7% of samples compared to normal tissues in tumor tissues, while increased expression was observed as 13.3%. Methylation was detected in all patients with decreased expression levels. While decreased expression was observed in 33.3% of tumor tissues having no methylation, increased expression was observed in 50%.

Discussion: It is thought that *GABRB3* gene may be responsible for a special subgroup of OSCC patients via methylation-related loss of expression and can be used as a potential biomarker candidate in early diagnosis and prognosis determination. Further studies in larger patient groups are needed to confirm these findings.

Key words: Oral squamous cell carcinoma, methylation, expression, biomarker

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Poster Presentation – 21

Investigation of Methylation and Expression Levels in *STK32C* Gene in Oral Malignant Lesions

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Introduction-Purpose: As a result of the array analyses obtained within the scope of the TUBITAK-SBAG-114S497 project conducted by Demokan and his colleagues, *STK32C* gene was determined as a potential epigenetic biomarker candidate. In this study, the methylation and expression levels of *STK32C* gene were examined in a larger patient group consisting of oral squamous cell carcinoma (OSCC) cases; the biomarker potential of this gene in terms of early diagnosis/prognostic evaluation was investigated.

Materials-Methods: DNA and RNA were isolated from tissue samples of 15 OSCC patients, and the methylation and expression levels of the *STK32C* gene were examined using Quantitative Methylation Specific PCR and Real-Time PCR methods, respectively.

Results: In tumor samples of OSCC patients, 93.3% methylation was observed in the promoter region of the *STK32C* gene. When expression levels were evaluated, expression loss was detected in 53.3% of the samples in tumor tissues compared to normal tissues, while expression increase was observed in 13.3%. Methylation was detected in all patients with decreased expression levels.

Discussion: It is suggested that the loss of expression observed in the *STK32C* gene due to methylation may play a role in the molecular characterization of a certain subgroup of OSCC patients and that this gene may be a significant biomarker candidate for early diagnosis and prognosis. However, further studies covering larger patient populations are needed to confirm this.

Key words: Oral squamous cell carcinoma, methylation, expression, biomarker

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Poster Presentation – 22

Tiroid Kanseri Hücre Hatlarında circPTPN22'nin Ekspresyonunun Araştırılması

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Giriş ve Amaç: PTPN22 (Protein tyrosine phosphatase non-receptor type 22), T hücre reseptörlerinin negatif regülatörü olarak bu hücrelerin homeostasinden sorumludur. Görevi gereği çeşitli otoimmün hastalıklar-özellikle otoimmün tiroid hastalığı- ve bazı kanser türleri ilişkilendirilmiştir. PTPN22 geninin ifadesini etkileyen yeni bir molekül ise circPTPN22'dir ve gerek gastrik ve pankreas kanserinde gerekse otoimmün hastalıklarda ifade değişikliği göstermekte olup potansiyel biyobelirteç olarak nitelendirilmektedir. Gerek halkasal formunun stabil olması gerekse kanda ve dokulardaki ifadesinden ötürü bu çalışmadaki amacımız circPTPN22'nin, PTPN22 mRNA'sı ile birlikte tiroid kanseri hücre hatları ile sağlıklı hücre hattı arasındaki ifade farklılıkları karşılaştırılarak biyobelirteç olma potansiyelini keşfetmektir.

Gereç ve Yöntemler: Bu çalışmada, tiorid kanseri hücre hattı olarak TPC-1 (insan papiller tiroid karsinom) ile FTC-133 (insan foliküler tiroid karsinom) ve sağlıklı kontrol hücre hattı olarak Nthy-ori 3-1 (insan tiroid foliküler epitel) kullanılmıştır. Elde edilen hücrelerden toplam RNA izolasyonu ve circRNA zenginleştirilmesi yapılmasının ardından cDNA'ya çevrilerek hem circPTPN22 hem de PTPN22 mRNA seviyesi qRT-PCR ile analiz edilmiştir. Referans gen olarak circRNA ifadelerinde circHIPK3, mRNA ifadelerinde ise GAPDH kullanılmıştır. Elde edilen sonuçlar, kat değişimini tespit etmek üzere $2^{-\Delta\Delta Ct}$ yöntemi ile değerlendirilmiştir.

Sonuçlar: Nthy-ori 3-1 ekspresyon değerine kıyasla, TPC-1 hücre hattında circPTPN22'nin relatif ekspresyon değeri 12,15; FTC-133 hücre hattında ise 4,43 kat arttığı belirlenmiştir; PTPN22 mRNA'sının relatif ekspresyon değeri TPC-1 hücre hattında 14,9; FTC-133 hücre hattında ise 3,57 kat artış olarak hesaplanmıştır. Bu bulgular, circPTPN22 ve lineer PTPN22'nin her iki tiroid kanseri hücrelerinde yüksek seviyelerde ifade edildiğini göstermekte ve circPTPN22 ile PTPN22 mRNA artışlarının birbirine paralel olduğu gözlenmiştir.

Tartışma: Bulgularımız, hem circPTPN22 hem de PTPN22 mRNA'sının ifadelerinin tiroid kanserinde her iki çeşit hücre hattında da arttığını göstermektedir. Gen ifadesinin kontrolünde circRNA-miRNA-mRNA eksini göz önüne alınacak olursa ara molekül miRNA belirlenmesi gelecek çalışmalarımızın hedefi olacaktır.

CircRNA'ların miRNA süngerlemesi yaparak mRNA ifadesini etkilediği bilindiğinden çalışmamızın sonuçları circPTPN22'nin tiroid kanserinde potansiyel bir biyobelirteç olarak değerlendirilebileceğini ortaya koymakla birlikte klinik örneklerde de teyit edilmesi elzemdir.

Anahtar Kelimeler: PTPN22 geni, circPTPN22, Tiroid Kanseri

Poster Presentation – 23

Staphylococcus epidermidis ile Enfekte Edilmiş Keratinosit Hücre Hattı ve Melanom Deri Kanseri Hücrelerinde Ultraviyole Işınların Kanserojen Etkileri

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Cilt kanseri büyük bir halk sağlığı endişesidir, melanom en agresif ve ölümcül formlardan biridir. Ultraviyole (UV) radyasyon, melanom için birincil çevresel risk faktörü olarak kabul edilir, bu da DNA hasarını, oksidatif stres ve bağışıklık baskılamasını indükler. UV maruziyetine ek olarak, son çalışmalar cilt mikrobiyotasının, özellikle Staphylococcus epidermidis'in kanser ilerlemesi ve modülasyonunda rol oynayabileceğini düşündürmektedir.

Bazı S. epidermidis suşları cilt neoplazisine karşı koruyucu etkiler sergilerken, diğerleri kanserle ilişkili mekanizmalarla ilişkilendirilmiştir. Bu çalışma, S. epidermidis enfeksiyonu ve UV radyasyonunun, hücresel yanıtlara ve potansiyel kanserojen etkileşimlere odaklanarak keratinositler ve melanom hücreleri üzerindeki etkilerini araştırmayı amaçlamaktadır.

Materyal ve Metot: Bu araştırmada, insan keratinosit (HACAT) ve melanom (SK-MEL-30) hücre dizileri standart koşullar altında kültürlendi ve S. epidermidis ile enfekte edildi. Bakteriyel enfeksiyondan sonra hücreler, fotohasar'a yanıtlarını değerlendirmek için kontrollü UV radyasyon dozlarına maruz bırakıldı. Daha sonra, toplam RNA izolasyonu ve cDNA sentezi ve qPCR prosedürü yapıldı. Bu yöntemlere bağlı olarak, kanser mekanizmasında rol oynayan ana genlerin gen ekspresyon seviyesinin belirlenmesi sağlandı. S. epidermidis ve UV maruziyetinin kansere bağlı yollar üzerindeki etkisini değerlendirmek için profil oluşturma, göç deneyleri ve hücre döngüsü analizi dahil olmak üzere çeşitli hücresel analizler yapıldı.

Sonuçlar: Bu çalışmanın sonuçları, cilt mikrobiyotası ile çevresel kanserojenler arasındaki etkileşime dair yeni bilgiler sunmakta ve melanom fizyopatolojisinde mikrobiyal katkıların daha iyi anlaşılmasına katkıda bulunmaktadır.

Tartışma: Elde edilen bulgular, cilt kanserinin önlenmesi ve tedavisinde mikrobiyal etkileşimleri hedef alan yeni terapötik stratejilerin geliştirilmesine yönelik önemli çıkarımlar sağlayabilir.

Anahtar Kelimeler: Cilt Kanseri, UV ışınları, Kanser, Bakteri, Tedavi.

Poster Presentation – 24

Tumor-associated Schwann cells decreased natural killer cell activity against pancreatic cancer cells

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Introduction: Natural Killer (NK) cells can eliminate early tumor cells, but their activity is suppressed by the tumor microenvironment. Nerves are known to contribute to the progression of pancreatic cancer, with Schwann cells playing a key role in mediating communication between nerves and cancer cells. Schwann cells may present in precancerous lesions and also can be reprogrammed by pancreatic cancer cells into a tumor-associated phenotype. In this study, we investigated how tumor-associated Schwann cells affect NK cell activity against pancreatic cancer cells.

Methods: Schwann cells were reprogrammed with PANC-1 CM, confirmed by GFAP expression. CM from Schwann and tumor-associated Schwann cells was applied to NK-92 cells, followed by 4-hour co-culture with Calcein-AM–labeled PANC-1 cells to assess cytotoxicity. IFN-γ secretion was measured by ELISA, and CellTracker dyes were utilized to assess NK-92 infiltration into PANC-1/Schwann spheroids.

Results: GFAP expression in Schwann cells treated with PANC-1 CM was twice that of controls. CM from both Schwann and tumor-associated Schwann cells reduced NK-92 cells cytotoxicity and IFN-γ secretion. Schwann cells within pancreatic cancer spheroids regulated NK-92 infiltration.

Discussion: In conclusion, tumor-associated Schwann cells suppressed NK-92 cytotoxicity through secreted factors, with specific molecules yet to be identified. Further research will explore these interactions and key factors.

Poster Presentation – 25

Temozolomid dirençli (T98G) ve duyarlı (U87) glioblastoma multiforme hücre hatlarında direnç gelişim sürecinin 2B *in vitro* kültür ortamında ozmotik basınç değişiklikleri ve ortamdaki seçilmiş elementlerin rolü açısından incelenmesi

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GBM en sık karşılaşılan sinir sistemi tümörü olarak bilinmektedir ve dünya çapında en sık görülen malign primer beyin tümörüdür. Tanı sonrasında 5 yıllık sağ kalım oranı %5'ten daha azdır ve medyan sağ kalım süresi 15 ay olarak bilinir. Progresyonsuz sağkalım süresi sadece 6 ay olarak rapor edilmesi ile en öldürücü kanser türlerinden biri olarak tanımlanmaktadır. Güncel GBM tedavisi; cerrahi müdahale başta olmak üzere hedefe yönelik tedavi, immünoterapi, adjuvan kombine radyasyon tedavisi ve alkilleyici ajan temozolomid (TMZ) ile kemoterapiyi bir arada kullanan yaklaşımları içermektedir. TMZ, imidazotetrazin sınıfı bir ön ilaç (pro-drug) olarak tanımlanmaktadır ve Guanine O^6 pozisyonunun metilasyonu yolu ile sitotoksik etki gösteren alkilleyici bir ajandır. Literatürde yer alan bilgiler doğrultusunda; TMZ'ye karşı gelişen direncin metil guanin metil transferaz (MGMT) enziminin aşırı ifadesi sonucu olduğunu gösterilmiştir. Fakat TMZ direnç mekanizmasında halen aydınlatılması gereken çok sayıda araştırma sorusu vardır. Bu noktada; hem direnç gelişim mekanizmanın farklı açılardan detaylandırılması hem de alternatif tedavi yaklaşımlarının geliştirilmesi oldukça önemlidir. Henüz klinik aşamada, GBM birinci basamak tedavisinde TMZ'ye alternatif sunulmamış olması bu alanda yürütülen çalışmaların önemini arttırmaktadır. Sunduğumuz bu çalışma kapsamında, U87 ve T98G hücre hatlarını farklı doz (10 µM, 20 µM, 30 µM, 100 µM, 500 µM) ve uygulama süreleri ile TMZ'ye maruz bırakarak U87'de TMZ direnç gelişim sürecini, T98G'de ise uygulama doz-süre kombinasyonunun etkisini ozmotik basınç ve seçili iyonların rolü özelinde inceledik. T98G ve U87 hücre hatları Dulbecco's Modified Eagle Medium (DMEM)- 10%v/v FBS & %1v/v penisilin-streptomisin içerisinde 2 farklı yaklaşım ile kültüre edildi. İlk olarak T98G ve U87 hücre hatları 100 µM ve 500 µM TMZ içerisinde 8-10 hafta süre ile sürekli olarak bırakıldı. İkinci yaklaşımda ise; başlangıç dozu olarak 10 µM, 20 µM, ve 30 µM seçilerek belirli aralıklar ile ortam değişikliği gerçekleştirildi ve uygulama dozları belirli aralıklar ile 2-katına çıkarılarak TMZ'ye maruz bırakıldı. Her iki TMZ doz-süre yaklaşımında, belirli zaman aralıklarında toplanan hücre ortam örneklerinden donma noktası prensibine dayalı olarak her örnekten 150 µL kullanılarak ozmotik basınç tayini gerçekleştirildi. Buna ek olarak, toplanan ortam örneklerinden İndüktif Eşleşmiş Plazma-Optik Emisyon Spektrometresi (ICP-OES) yaklaşımı ile kalsiyum, potasyum ve sodyum elementlerine ait miktar tayini gerçekleştirildi. Sonuç olarak doz-süre ve uygulama yaklaşımı spesifik olarak değişen 2B *in vitro* kültür ortam içeriğinin direnç gelişim sürecindeki rolünü moleküler seviyede inceleyerek olası biyobelirteç hedeflerinin tanımlanmasını hedefleyen veriler elde edildi.

Anahtar Kelimeler: Glioblastoma Multiforme; Temozolomid; Kemoterapötik Direnci; Ozmotik Basınç; İndüktif Eşleşmiş Plazma-Optik Emisyon Spektrometresi

Investigation of Autophagy-Associated VPS34 Inhibitor Via Wnt/B-Catenin Signaling Pathway in Pancreatic Cancer Cell Line

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Introduction and Aim: Pancreatic ductal adenocarcinoma (PDAC) is a challenging cancer type with limited treatment options, often diagnosed at advanced stages. Many molecular mechanisms are known to be involved in PDAC cell development, including autophagy. Autophagy plays a role in cancer cell resistance and aggressiveness. Also, it has complex interactions with the Wnt/β-catenin signaling pathway, which is one of the other dysregulated mechanisms in PDAC. We aimed to understand how inhibiting autophagy affects the Wnt/β-catenin signaling pathway and its anti-cancer effects in PDAC. Materials and Methods: PANC-1 and MIA PaCa-2 PDAC cell lines were used. According to our purpose, VPS34, one of the primary regulators of autophagy, was targeted and inhibited with autophinib, and cell viability was examined by WST-8/CCK8 assay. To investigate the potential interaction between the autophagy and Wnt/β-catenin signaling pathway, the expression levels of target genes were analyzed by qRT-PCR. To analyze the autophagy and apoptosis level LC3-II ELISA kit and Human CASP3 (Caspase 3) ELISA kit were used. Results and Discussion: Inhibiting autophagy can promote the destruction of cancer cells. According to this theory, suppressing autophagy pathways reduced the survival of the cells and caused the PDAC cells to undergo apoptosis. Findings indicate that targeting autophagy in PDAC cells can impact Wnt/β-catenin signaling synergetically, promote apoptosis, and potentially offer therapeutic benefits in pancreatic cancer treatment.

Key words: Autophagy, Pancreatic ductal adenocarcinoma (PDAC), VPS34, Wnt/β-catenin Signaling Pathway

Poster Presentation – 27

Meme kanseri hücreleri lipoprotein içermeyen ortamda aerobik glikolizi baskılar

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Giriş ve Amaç: Kanser hücrelerinde metabolik yolaklar ATP üretimini arttıracak şekilde yeniden düzenlenir. Kolesterol, normal hücre büyümesi ve çoğalması için gerekli olan bir non-esansiyel metabolittir. Çoğalan hücrelerde yeni membranların yapılabilmesi, hücre sinyal ileti sisteminin aktif bir şekilde devam edebilmesi için endojen kolesterol sentezine ve dışarıdan lipid partiküllerinin alınmasına ihtiyaç vardır. Kolesterol, kansere yönelik keşfedilecek biyobelirteçler ile anti-kanser tedavilerin geliştirilmesi için bir hedef olabilir. Çalışmanın amacı, kanser hücrelerinin kolesterol olmayan ortamda verdikleri hücresel yanıtın incelenmesidir.

Materyal ve Metot: Fetal bovin serum (FBS) içeren ya da Lipoprotein içermeyen (LPDS) besiyerinde büyütülen MCF-7 ve MDA-MB-231 hücrelerinin canlılık analizleri MTT yöntemi kullanılarak gerçekleştirildi. LC-MS analizi için, MDA-MB-231 hücreleri ($3x10^5$/3ml) FBS ya da LPDS içeren besiyerinde 96 saat inkübe edildikten sonra tripsinize edilerek literatürde belirtildiği şekilde ekstrakte edildi (1). Her numune grubundan 5 µl süpernatant, pozitif ve negatif iyonizasyon modları için ayrı enjeksiyonlara tabi tutuldu. Data analizi untargeted metabolomiks sonuçlarına göre yapıldı.

Sonuçlar: LPDS içerikli besiyerinde her iki hücre hattının canlılığı azalırken, bu azalış MDA-MB-231 hücrelerinde daha fazla gözlendi. LPDS içeren besiyerinde inkübe edilen hücrelerde, gliserol-3-fosfat ve pirüvik asit seviyeleri anlamlı düzeyde artarken ($p^{***} < 0.001$), laktik asit ve alfa ketoglutarat seviyeleri anlamlı düzeyde azaldı ($p^{***} < 0.001$).

Tartışma: LPDS içeren ortamda, glikolizin bir ara ürünü olan gliserol-3-fosfat birikimi, aerobik glikolizin azalmış olabileceğini düşündürmekte, laktik asit seviyesinin azalması da bunu desteklemektedir. Trikarboksilik asit (TCA) döngüsünde rol alan bir ürün olan pirüvik asit seviyesindeki artış ise hücrelerin TCA döngüsüne giriyor olabileceğine işaret etmektedir. TCA döngüsünün bir ara ürünü olan alfa ketoglutarat seviyesinde görülen azalış, bu metabolitin tüketildiğine, dolayısıyla TCA döngüsünün aktifleştirildiğine yönelik kanıyı güçlendirmektedir. Bu çalışma, meme kanseri hücrelerinin kolesterol yokluğunda metabolik yeniden düzenleme sürecine girerek, aerobik glikolizin baskılandığını ve TCA döngüsünün öncelikli metabolik yol olarak tercih edildiğini gösteren ilk verileri ortaya koymaktadır.

Anahtar kelimeler: Biyobelirteç, kolesterol, lipid, membran, metabolizma

Kaynaklar

1. Breitkopf SB, Ricoult SJH, Yuan M, Xu Y, Peake DA, Manning BD, Asara JM. A relative quantitative positive/negative ion switching method for untargeted lipidomics via high resolution LC-MS/MS from any biological source. Metabolomics. 2017 Mar;13(3):30.

Epidermal growth factor and androgen receptors dual targeting by osimertinib and enzalutamide reversed epithelial-mesenchymal transition and induced apoptosis in glioblastoma cell lines

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Introduction & Aim: Glioblastoma (GBM) is an aggressive brain tumor with poor survival rates. Epithelial-mesenchymal transition (EMT) is a reversible biological process characterized by increased cell motility and resistance to chemotherapeutic agents. The mutations and the enhanced activity of epidermal growth factor receptor (EGFR) are common in GBM. Recent studies have reported that androgen receptor (AR) is overexpressed in GBM. A direct interaction of EGFR and AR was shown in cancer cells. Osimertinib (OSI) is a compound to target EGFR and induces apoptosis while enzalutamide (ENZ) is used to hamper AR expression. We aimed to examine the dual effect of OSI and ENZ in GBM, focusing on EMT and apoptosis signaling pathways.

Methods & Materials: MTT assay was conducted to evaluate the impacts of OSI and/or ENZ in LN18, U87, and HMC3 cell lines. Fluorescence microscopy was performed to visualize the effects of OSI and ENZ on cell membrane, chromatin condensation and cell death. The 3D colony formation potential was performed by hanging drop. The migration potential of GBM cells exposed to OSI and ENZ was assessed using a scratch assay. Finally, expression profiles of EMT and apoptotic markers were detected by immunoblotting.

Results: OSI and ENZ co-treatment dramatically increased the cell viability loss in LN18 and U87 cells, however this effect was not detected in HMC3 cells. The 3D colony formation potential was hindered upon combined treatment with OSI and ENZ. The combination of OSI and ENZ slowed down the migration potential of LN18 and U87 cells. Epithelial and apoptotic marker expression levels were enhanced while mesenchymal marker expression was diminished.

Discussion: These findings proposed that the combination of OSI and ENZ suppresses EMT and promotes apoptosis in LN18 and U87 glioblastoma cell lines.

Key words: Glioblastoma, epidermal growth factor receptor, androgen receptor, osimertinib, enzalutamide, epithelial-mesenchymal transition

Targeting Nicotinamide N-methyltransferase to Overcome Taxane Resistance in Castration-Resistant Prostate Cancer

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Introduction Aim: Castration resistant prostate cancer (CRPC) is defined by its resistance to conventional hormone therapies. At this stage, chemotherapeutic agents such as Docetaxel (Dtx) and Cabazitaxel (Cbz) remain the primary treatment options. However, resistance to taxanes significantly limits therapeutic efficacy, necessitating the identification of novel molecular targets to overcome this challenge. The aim of this study is to identify key molecular players driving taxane resistance in CRPC. Among the candidates identified through transcriptomic and proteomic analyses, nicotinamide N-methyltransferase (NNMT) emerged as a potential contributor. Additionally, NNMT has a known function as a methyl sink, consuming S-adenosyl methionine and reducing the cellular methylation potential. We hypothesized that this may alter histone methylation marks and contribute to the epigenetic regulation of chemoresistance, with NNMT acting as an indirect epigenetic regulator.

Materials & Methods: We established Dtx- and Cbz-resistant DU145 PC cell lines to uncover vulnerabilities associated with taxane resistance. Transcriptomic profiling using RNA sequencing revealed differential gene expression, while proteomic analysis via NanoLC-MS/MS identified protein-level alterations between resistant and parental cells. Gene and protein expression changes were validated by RT-qPCR and Western blotting, respectively. To investigate the functional relevance of NNMT, we performed knockdown, knockout, and overexpression experiments, and assessed taxane sensitivity using SRB and clonogenic assays. Considering NNMT's role as a methyl sink, its potential link to epigenetic regulation was examined by analyzing H3K4me3 and H3K27me3 levels following histone extraction. Publicly available clinical PC datasets were analyzed using cBioPortal for Cancer Genomics.

Results: Among the significantly upregulated genes, NNMT emerged as a top upregulated gene/protein. Overexpression of NNMT in two different CRPC parental cell lines conferred taxane resistance, while its silencing or knockout restored taxane-sensitivity in resistant cells. Supporting this, clonogenic survival assays demonstrated that pharmacological inhibition of NNMT (1-MNA) re-sensitized DU145-derived taxane-resistant cells (DU145-DtxR and DU145-CbzR) to taxanes.

Notably, NNMT inhibition did not affect taxane response in parental cells, suggesting a resistance-specific function. Furthermore, NNMT knockout resulted in altered histone modification patterns, with increased H3K4me3 and H3K27me3 marks, indicating a potential role in epigenetic regulation. NNMT expression was also elevated in clinical CRPC datasets, with higher levels correlating with increased

Gleason scores and lymph node metastasis.

Discussion: This study demonstrates that NNMT may serve as a novel molecular target in overcoming taxane resistance in CRPC. Supported by clinical data, these findings suggest that NNMT could be considered both a biomarker and a potential therapeutic target in advanced PC.

Key words: NNMT, Chemoresistance, Epigenetic, Taxane.

Palladium(II)-Barbiturate Complex: A Promising Treatment Option for BRAF-mutant Colorectal Cancer

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Colorectal cancer (CRC) is one of the most commonly diagnosed cancers in adults, considering both its incidence and prevalence. KRAS and BRAF mutations are the most common mutations observed in CRC, and there is no standard treatment option specifically determined for BRAF mutant tumors. Palladium complexes have gained attention in cancer treatment due to their promising properties. This study evaluated the antigrowth/cytotoxic effect of Pd(II) complex to provide an effective treatment modality for KRAS and BRAF-mutant CRC cells. The anti-growth effect of the Pd(II) complex evaluated on HCT15 (KRAS-mutant) and HT29 (BRAF-mutant) cell lines using luminescent ATP assay in vitro. Cell death mode was determined by flow cytometry and western blotting. The anti-migration, anti-invasion, and anti-angiogenic properties of Pd(II) complex were investigated. Moreover, CD 1 Nude Mouse models were established, and antitumor effects were also examined in vivo. Pd(II) complex showed anti-growth effects against both cell lines in vitro depending on the dose and time, and showed a strong anti-tumor effect, especially on BRAF-mutant tumors in vivo. It was found that Pd(II) complex caused apoptosis in CRC cells via DNA damage together with ROS increase. At the same time, it was seen that migration, invasive, and angiogenic abilities were inhibited in both cell lines. After Pd(II) complex treatment, a decrease in protein expressions supporting cell proliferation and resistance was detected. In conclusion, the Pd(II) complex shows promise as a possible treatment option for aggressive CRC tumors with BRAF mutations, which are currently being researched in animal models by our group.
Key words: Colorectal cancer, BRAF mutation, Palladium, Personalized medicine

Poster Presentation – 31

Apoptotic Molecular Mechanism of Protein-rich *Macrovipera Lebetinus* Snake Venom in

Colorectal Cancer Cells in Turkiye

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Introduction and Aim: According to the International Agency for Research on Cancer (IARC) data published in 2022, colorectal cancer is a fatal disease that ranks fourth in incidence rate and fifth in mortality rate among cancers worldwide, regardless of gender [1-3]. In this study, it was aimed to develop an alternative or complementary treatment method against colon tumours resistant to treatments due to mutated KRAS, BRAF, FAS and TRAIL genes by treatment of snake venom with rich peptide content of *Macrovipera lebetinus* (M. lebetinus) species belonging to the most venomous *Viperidae* family of Turkiye.

Materials and Methods: M. lebetinus snake venom collected from Soğmatar village of Şanlıurfa province was powdered by lyophilisation. The cytotoxicity analysis of the venom was compared on DLD-1 and CCD-18Co cell lines by Alamar Blue method. The apoptotic effect on DLD-1 cell line was determined by flow cytometry method using Annexin V-APC and 7-AAD dyes. Western blot and qRT-PCR methods were used to evaluate the effects at molecular level.

Results: The IC50 values of DLD-1 and CCD-18Co cells were calculated as 6.12 µg/mL and 15 µg/mL, respectively. Venom altered the rate of early apoptosis (13.07%) and late apoptosis (0.96%) in colon cancer cells. In the human apoptosis panel gene study, it increased the expression of 74 genes and decreased the expression of 4 genes. In human colon cancer panel gene study, it decreased the expression of 72 genes and increased the expression of 1 gene. In protein expression studies, venom decreased BCL-2 (0.56-fold) protein expression and increased P53 (1.08-fold) and BAX (1.25-fold) protein expressions in DLD-1 cell line.

Discussion: M. lebetinus snake venom is thought to be an alternative or complementary agent that reduces resistance and responds to treatment by altering effective gene and protein mechanisms in colon cancer.

Key words: Macrovipera lebetinus, Colorectal cancer, Apoptosis, Gene and protein expression

References

1.Ferlay, J., et al., Cancer statistics for the year 2020: An overview. International journal of cancer, 2021. 149(4): p. 778-789.

2. Sung, H., et al., Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians, 2021. 71(3): p. 209-249.

3. Wéber, A., et al., Global burden of bladder cancer mortality in 2020 and 2040 according to GLOBOCAN estimates. World Journal of Urology, 2024. 42(1): p. 1-10.

Poster Presentation – 32

Activation of Apoptotic Pathways in Colon Cancer Cells: Effects of *Apis Mellifera Anatoliaca* Venom at the Gene and Protein Levels

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Colon cancer is one of the most common types of cancer worldwide and necessitates the development of innovative treatments. Bee venom is a natural apitherapeutic agent used to treat diseases and tumors related to the immune system. One of the crucial biological compounds in Bee venom is Melittin inhibits the growth of tumor cells by stopping the cell cycle and leading to apoptosis[1]. This study aimed to investigate the effects of bee venom of *Apis Mellifera Anatolica* on human colon cancer cells at the molecular level and to evaluate the role of these effects on genes and proteins in the apoptotic pathway. The bee venom was obtained from *Apis mellifera anatoliaca* hives in Manisa, Türkiye. Glass plates were placed in the hives where the bees were kept, and a 12.5 V electric current was applied to encourage the bees to sting the glass[2]. For molecular changes in the apoptotic pathway, mRNA expression of 88 key genes involved in the apoptotic pathway was evaluated. A total of 32 genes were upregulated and 6 genes were downregulated (threshold set at a 2-fold change). Protein expression levels of apoptosis-related markers such as Bax, P53, Caspase-3, Caspase-9, and Caspase-12 were then analyzed using Western blotting. Bee venom treatment significantly increased pro-apoptotic protein expressions (Bax: $p<0.001$, p53: $p<0.001$, Caspase-3: $p<0.0001$, Caspase-12: $p<0.0001$) while significantly decreasing anti-apoptotic protein expressions (Bcl-2: $p<0.0001$). In conclusion, bee venom of *Apis mellifera Anatolica* may be used as a therapeutic agent for the treatment of the colon cancer in combination with conventional treatments.

Key words: *Apis mellifera anatoliaca,* Bee venom, Colon cancer, Apoptotic pathway, Gene/protein expression.

References:

1. Wang, C., Chen, T., Zhang, N., Yang, M., Li, B., Lu, X., Cao, X., & Ling, C. (2009). Melittin, a major component of bee venom, sensitizes human hepatocellular carcinoma cells to tumor necrosis factor-related apoptosis-inducing ligand (TRAIL)-induced apoptosis by activating CaMKII-TAK1-JNK/p38 and inhibiting IκBα kinase-NFκB. *Journal of Biological Chemistry*, *284*(6), 3804-3813.
2. Benton, A. W., Morse, R. A. ve Stewart, J. D., 1963, Venom Collection from Honey Bees, *Science*, 142 (3589), 228-230.

Poster Presentation – 33

Investigation of the Antioxidant Analyses of Anatolian Saffron and Its Cytotoxic Effects on Prostate Cancer Cells

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Prostate cancer is one of the most aggressive and fatal types of tumors. The development of new therapeutic drug candidates is crucial for its treatment. Saffron (Crocus sativus L.) is a medicinal plant with pharmacological properties due to its secondary metabolites, such as crocin, picrocrocin, and safranal (1). In this study, in addition to analyzing the total phenolic, flavonoid, and antioxidant capacities of saffron extract, the cytotoxic effects of silver nanoparticles (AgNPs) synthesized via green synthesis on prostate cancer cells were investigated. For extract preparation, 1 mg of saffron was incubated in 1 mL of deionized water (dH_2O) at 60°C for 24 hours. The antioxidant capacity of the aqueous extract was determined using the DPPH and CUPRAC methods. AgNPs were synthesized using the saffron extract as a reducing agent, and their characterization was performed via UV-Vis spectrophotometry and dynamic light scattering (DLS). The cytotoxic effect of AgNPs on human prostate cancer cells (LNCaP) was assessed using the Alamar Blue assay. The total phenolic content of the saffron aqueous extract was determined as 153.16 ± 0.03 mg GAE/g, while the flavonoid content was 1059.218 ± 0.003 mg QE/g. The IC_{50} value for DPPH activity was 10.60 ± 0.2 µg/mL, and the A0.50 value for CUPRAC was 0.313 ± 0.4 µg/mL. The synthesized AgNPs exhibited maximum absorbance at 410 nm in the UV-Vis spectrophotometer and had an average size of 54 nm based on DLS analysis. The IC_{50} value of the silver nanoparticles synthesized from saffron on PC-3 cells was calculated as 25.34 ± 1.2 µg/mL. These findings demonstrate that saffron is an effective reducing agent for green synthesis of silver nanoparticles, which are widely used in various fields. Additionally, the antioxidant activity of saffron contributes to inhibiting cancer cell growth. Therefore, saffron holds potential as a natural therapeutic agent for use in both healthcare and industrial applications.

Key words: Saffron (*Crocus sativus* L.), Silver nanoparticles (AgNPs), Green synthesis, Prostate cancer, Cytotoxicity

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References:

1. Çinar, A. S., & Önder, A. (2019). Anadolu'nun kültürel mirası: Crocus sativus L.(Safran). *FABAD Journal of Pharmaceutical Sciences*, *44*(1), 79-88.

Poster Presentation – 34

Investigation of the Anti-Cancer Effects of Stypopodium schimperii and Its Potential for Commercial Use

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One of the invasive brown algaes, *Stypopodium schimperii* is known to have beneficial effects on human health due to its bioactive polysaccharide content, including alginate, laminarin, and fucoidan, which exhibit anti-cancer properties particularly on colorectal cancer. This study aims to investigate the anti-cancer effects of *S. schimperii* and evaluate its potential for commercial applications. Macroalgae samples from summer and autumn were washed, oven-dried at 40 °C, and powdered (20 g). They were extracted with 80% methanol (200 mL × 3) by maceration at room temperature. The combined filtrates were evaporated under reduced pressure, dissolved in distilled water, and lyophilized. Methanol extracts of *S. schimperii* obtained in summer and autumn (SCHSM, SCHAM) were assessed for their cytotoxic effects on the colorectal cancer (hCRC) cell line HT-29 and the healthy colorectal cell line CCD-18Co using the Alamar Blue assay. Changes in the mRNA expression of key genes involved in the hCRC molecular pathway were analyzed using the Human Colon Cancer Primer Library Panel and qRT-PCR. The IC_{50} values of SCHSM and SCHAM for HT-29 cells were determined as 48.71 µg/mL and 60.86 µg/mL, respectively, whereas for the healthy CCD-18Co cells, the IC_{50} value was calculated as 200 µg/mL. qRT-PCR analysis revealed that the expression levels of *TP53, BMP4,* and *MSH6* increased 2.57-fold, 3.95-fold, and 12.77-fold, respectively, in the SCHSM group, while in the SCHAM group, their expression increased 2.56-fold, 6.37-fold, and 14.22-fold, respectively. Conversely, the expression levels of *CTNB1, EGFR,* and *WNT5* decreased by 8.27-fold, 10.27-fold, and 34.36-fold, respectively, in the SCHSM group, and by 5.91-fold, 6.72-fold, and 38.62-fold, respectively, in the SCHAM group. These findings indicate that *Stypopodium schimperii* exerts significant anti-cancer effects on hCRC cells and may serve as an alternative strategy for cancer treatment as a novel therapeutic agent in cancer treatment.

Key words: *Stypopodium schimperii*, İnvasive Brown Algae, Colorectal Cancer, Cytotoxicity, Therapeutic Potential.
Acknowledgment: This study was supported by TUBITAK (Project number: 124Y004)
Poster Presentation – 35

Pro-Apoptotic and Oncogene-Suppressing Effects of *Stypopodium schimperii* Extracts on Human Colorectal Carcinoma

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Stypopodium schimperii, an invasive brown algae species, not only poses negative effects on marine ecosystems but also offers potential health benefits. This study aims to investigate the anti-carcinogenic effects of S schimperii on human colorectal carcinoma (hCRC). Ethanol extracts of S. schimperii collected in autumn and summer (SCHAE and SCHSE) were evaluated for their cytotoxic effects on the hCRC cell line; DLD-1 and the healthy colorectal cell line; CCD-18Co. Macroalgae samples collected in summer and autumn were washed and dried in an oven at 40 °C. The powdered samples (20 g) were extracted with 80% ethanol (200 mL x 3 times) by maceration at room temperature. Cytotoxicity assays performed using the Alamar Blue test revealed that SCHAE and SCHSE extracts exhibited IC_{50} values of 60.0 µg/mL and 71.0 µg/mL, respectively, against the DLD-1 cells. On the other hand, the IC_{50} value was determined to be higher than 200 µg/mL in healthy colon cells. Additionally, the mRNA expressions of genes involved in colorectal cancer at the molecular level were analyzed using qRT-PCR. The mRNA expressions of AXIN1, ACVR2A, and BMPR2 increased by 2.7-fold, 2.5-fold, and 3.0-fold, respectively, in the SCHAE group. Similarly, their expression levels increased by 2.3-fold, 46.3-fold, and 2.3-fold in the SCHSE group. On the other hand, the mRNA expressions of TYMS, MYC, and ALX4 decreased by 2.5-fold, 9.2-fold, and 61.5-fold, respectively, in the SCHAE group. In the SCHSE group, they decreased by 4.8-fold, 18.3-fold, and 62.0-fold, respectively. These results indicate that Stypopodium schimperii possesses significant anti-cancer activity against hCRC, suggesting that this algae species could serve as a potential strategy for cancer treatment.
Key words: Stypopodium schimperii, Anti-carcinogenic activity, Colorectal cancer, Cytotoxicity, Gene expression.
Acknowledgment: This study was supported by TUBITAK (Project number: 124Y004)

Poster Presentation – 36

Resveratrol-induced cytotoxicity in colorectal cancer: Influence of microsatellite stability

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Introduction and Aim: Colorectal cancer (CRC) is an aggressive malignancy and the second leading cause of cancer- related deaths worldwide. Approximately %85 of CRC patients are classified as microsatellite stable (MSS), while the rest exhibit microsatellite instability (MSI), which is associated with a better prognosis and survival. Although, chemotherapy, surgery, and targeted therapies are commonly used to treat CRC, interest in phytotherapy, use of plant-derived compounds, is growing. Resveratrol, a natural polyphenol found in foods like grapes, red wine and berries, has demonstrated anticancer effects on CRC cells and may enhance chemotherapy efficacy by inhibiting pro-angiogenic and inflammatory pathways. Here, we aimed to investigate the cytotoxic and tumor-suppressive effects of resveratrol in MSI and MSS CRC cell lines.

Materials and Methods: To test the possible cytotoxic effect of resveratrol, different CRC cell lines representing MSS (SW480, HT29, SW837) and MSI (HCT116, HCT15) patient profiles were used in *in vitro* settings. Cells were seeded on 96-well plates and were treated with different doses of resveratrol ranging from 0 to 200 μM for 72 h. Cell viability was determined by using the Sulforhodamine B (SRB) assay.

Results: Our findings indicate that MSI CRC cells (HCT15 and HCT116) exhibited comparably lower %50 inhibitory concentration (IC50) values as compared to MSS CRC cells (HT29, SW480 and SW837), suggesting selective cytotoxicity based on microsatellite status. This further shows that MSI cells demonstrate greater sensitivity to resveratrol.

Discussion: Our study suggest that resveratrol exhibits selective cytotoxicity in CRC cells based on microsatellite stability. Lower IC50 values in MSI cells may be attributed to genetic variations, such as defective DNA mismatch repair, enhancing their susceptibility to drug. Overall, these results highlight resveratrol's potential as a targeted therapy for MSI CRC, warranting further research to elucidate the underlying molecular mechanisms and clinical relevance.

Key words: Colorectal cancer, microsatellite stability, resveratrol

Poster Presentation – 37

Effects of Iurus kinzelbachi Scorpion Venom on mTOR and MAPK Pathways in Human Colorectal Carcinoma

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Colorectal cancer (CRC) is the third leading cause of death with high mortality and morbidity rates in men and women worldwide (1). Although colon cancer is the most important cancer- related death, there are some therapeutic options for this disease. Severe side effects or inadequacy of these therapeutic treatment strategies make it inevitable to search for new and alternative treatment methods. One of these sources is scorpion venom has been thought to be an important drug candidate for medical applications. The potential of peptides and proteins contained in scorpion venoms isolated from various scorpion species to be used in the treatment of many diseases, especially cancer. In this study, it was aimed to investigate the effects of scorpion venom belonging to *Iurus kinzelbachi* species on the pathways involved in the development of human colon cancer. The *Iurus kinzelbachi* scorpion species was collected from Adana and venoms were milked using 12V electricity. Its cytotoxic effects on human colon cancer DLD-1 cell line and healthy colon epithelial cell CCD-18Co were determined by the Alamar Blue method, and mRNA expression was determined by qRT-PCR method using a colon cancer panel. Scorpion venom had an IC50 value of 20.86 (µg/mL) on DLD1 cells, while an IC50 value was determined as 250 (µg/mL) against CCD18Co cells. It was observed that *mTOR*, *MAPK3* and *TP53* mRNA expressions were decreased as 5.01-fold, 3.7-fold, and 7.5- fold, respectively. On the other hand, the mRNA expression of the *MAPK1* was increased 3.7- fold following venom treatment. No change was detected in the mRNA expression of the *MAPK8*. In conclusion, it has been evaluated that scorpion venom may have an important role in the treatment of colon cancer due to its selective effect and regulating effect on the molecular mechanism of cancer.

Key words: *Iurus kinzelbachi*, scorpion venom, colon cancer, pathway analysis
Acknowledgment: This study was funded by Scientific and Technological Research Council of Türkiye (TÜBITAK). The project number is 120Z942.

Reference:

1. Granados-Romero, J. J., Valderrama-Treviño, A. I., Contreras-Flores, E. H., Barrera-Mera, B., Herrera Enríquez, M., Uriarte-Ruíz, K., ... & Arauz-Peña, G. (2017). Colorectal cancer: a review. *Int J Res Med Sci*, *5*(11), 4667.

Poster Presentation – 38

Taraxacum officinale ve Leontice leontopetalum L. Ekstrelerinin Antioksidan ve Sitotoksik Aktiviteleri

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Giriş: İnsanoğlu, tarih boyunca yaşam standartlarını yükseltmek ve hayatta kalma şanslarını artırmak amacıyla doğal kaynaklar arayışında bulunmuşlardır. Toplumların gelişmesiyle birlikte bitkiler, insan aracılığıyla önemli bir terapötik kaynak haline gelmiştir, çünkü biyolojik olarak sınırsız işlevsel maddeler içermektedir. Bu maddeler, insanları etkileyen çeşitli hastalıkların tedavisi ve ilişkili komplikasyonların önlenmesi/düzeltilmesi için önemlidir.

Taraxacum officinale geleneksel tıpta piroz, karaciğer, böbrek ve cilt hastalıkları durumunda bir çare olarak uzun süredir kullanılmaktadır. Antioksidan, antienflamatuar, antianjiyojenik, antinosiseptif etkiler nedeniyle sürekli araştırma altında olan 100'den fazla biyoaktif bileşen içerir. *Leontice leontopetalum* L. bitkisi, halk arasında kan durdurucu olarak kullanılmakta ve çiçeklenme döneminde toprak üstü kısımları meme, rahim, lenf bezi ve prostat kanserlerine karşı koruyucu olarak çay şeklinde tüketilmektedir.

Yöntem: Bu çalışmada, iki bitkinin farklı yöntemlerle elde edilen ekstraktlarının insan akciğer, karaciğer ve pankreas hücre hatları üzerindeki antitümör etkileri ve antioksidatif etkinlikleri değerlendirilmiştir. Bu amaçla sitotoksik değerlendirme için SRB testi, antioksidan aktivite için DPPH ve CUPRAC testleri seçilmiştir.

Sonuç ve Tartışma: İki bitki türünün bitki ekstraksiyon yöntemine, ekstrakt konsantrasyonuna, bitkinin kullanılan bölümüne bağlı olarak değişen sitotoksik aktivite gösterdikleri ortaya konmuştur.

Anahtar Kelimeler: Taraxacum officinale, Leontice leontopetalum, Sitotoksik Aktivite, Antioksidan

Poster Presentation – 39

Investigation of the Effects of Zinc-Borate Treatment on The Lipid Metabolism of SW480 and SW620 Colorectal Cancer Cells

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Introduction and Aim: Free fatty acids generated in excess amount often stored in the form of lipid droplets. Deregulation of lipid metabolism and enhanced lipid droplet formation is known to contribute to the progression of cancer as energy supply when nutrients are scarce as well as a source of plasma membrane building block. Boron derivatives have been shown to affect lipid metabolism of cells through induction of lipophagy and effecting the expression of fatty acid transporters. The scope of the study is therefore to investigate the effect of zinc-borate (ZnBor) treatment on lipid metabolism of primary (SW480) and metastatic (SW620) colorectal cancer (CRC) cells.

Materials and Methods: MTT assay assessed ZnBor cytotoxicity and determined experimental doses. Nile Red staining evaluated lipid droplet changes, while the colony formation assay examined ZnBor's effects alone or with AZD-8055 (autophagy inducer), 6-AN, and AG-120 (cytoplasmic NAPDH generation inhibitors) on cell proliferation by modulating lipophagy and fatty acid availability.

Results: ZnBor concentrations of 200µM and 750µM were selected based on their ability to support high and moderate cell viability, respectively. While ZnBor alone did not significantly alter lipid droplet content, it reduced lipid accumulation under L-glutamine deprivation. SW480 cells exhibited high sensitivity to ZnBor, limiting combinatorial effects, whereas SW620 cells showed a significant decrease in colony formation when treated with ZnBor and AZD-8055, particularly under glutamine starved cells.

Discussion: ZnBor reduced lipid droplet accumulation under L-glutamine deprivation, suggesting a role in lipid metabolism regulation. While SW480 cells showed high sensitivity to ZnBor alone, SW620 cells exhibited a significant decline in colony formation when combined with AZD-8055, especially under glutamine withdrawal. This highlights the potential of metabolic stress and mTOR inhibition in targeting aggressive CRC, warranting further investigation.

Key words: Colorectal cancer, lipid metabolism, zinc-borate

References:

1. Şahin, E., Orhan, C., Erten, F., Şahin, F., Şahin, N., C Şahin, K. (2023). The effect of different boron compounds on nutrient digestibility, intestinal nutrient transporters, and liver lipid metabolism. *Turkish Journal of Medical Sciences*, 53(3), 619–629. https://doi.org/10.55730/1300-0144.5624

2. Aysan, E., Sahin, F., Telci, D., Erdem, M., Muslumanoglu, M., Yardmc, E., C Bektasoglu, H. (2013). Mechanism of Body Weight Reducing Effect of Oral Boric Acid Intake. *International Journal of Endocrinology*, *2013*, 914651. https://doi.org/10.1155/2013/914651

Poster Presentation – 40

Natural compounds in cancer therapy: the role of curcumin and bromelain in triple-negative breast cancer

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Introduction and Aim: Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer (BC) lacking estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2), limiting treatment options. Curcumin, a turmeric-derived compound, and bromelain, a proteolytic enzyme extracted from pineapple, are two plant-derived compounds with promising anticancer activities across various cancer types, including BC. Bromelain induces apoptosis, enhances drug absorption and modulates immunity, while curcumin primarily disrupts cancer cell signaling. This study investigates their potential synergistic cytotoxic effects on a TNBC cell line, MDA-MB-231.

Materials and Methods: Cells were treated with varying doses of curcumin and bromelain for 72 hours to evaluate individual cytotoxicity. Subsequently, the two agents were administered in combination at different concentrations, based on their respective 50% inhibitory concentrations (IC50). Cell viability was measured using the Sulforhodamine B (SRB) assay and colony formation assays evaluated long-term antiproliferative effects.

Results: Both agents demonstrated significant dose-dependent inhibition of cell growth, with IC50 values of 79.3 μg/ml for bromelain and 20.6 μM for curcumin. Similar results were observed in the combination-treated cells, suggesting that the combination therapy did not cause a clear synergistic effect compared to monotherapies. Instead, the antiproliferative effect achieved through the combined treatment of both compounds was possibly due to an additive effect. In the colony formation assay, the near-complete elimination of colonies in the high-dose single-agent groups confirmed that the long-term proliferative capacity of the cells was actively suppressed.

Discussion: Although the combination treatments did not exhibit a pronounced synergistic effect, both compounds demonstrated significant antiproliferative activity when administered individually. Considering their known roles in modulating oxidative stress, inflammation, and apoptotic pathways, the observed inhibitory effects on long-term cell proliferation are biologically relevant. These findings suggest that further studies are warranted to comprehensively evaluate the therapeutic potential of combining these agents.

Key words: Curcumin, Bromelain, Triple-negative breast cancer

Poster Presentation – 41

Staphylococcus aureus Enfeksiyonunun Akciğer Kanseri ve Normal Bronşiyal Hücreler Üzerindeki Farklı Etkileri

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Giriş ve Amaç: Staphylococcus aureus (S. aureus) enfeksiyonu, akciğer kanseri hastalarında yaygın görülen bir komplikasyon olup, enfeksiyon kaynaklı problemlerin %70'ine kadar ulaşabilmektedir. Ekstraselüler bir patojen olan S. aureus'un tümör dokularında hayatta kalabildiği ve çoğalabildiği gösterilmiştir. Kanser tedavilerine rağmen bu tür enfeksiyonlar önemli bir mortalite nedeni olmaya devam etmektedir. Çalışmamız, S. aureus enfeksiyonunun akciğer kanseri ve normal bronşiyal epitel hücreleri üzerindeki moleküler ve hücresel etkilerini incelemeyi amaçlamaktadır.

Gereç ve Yöntemler: A549 akciğer kanseri ve BEAS-2B bronşiyal epitel hücre hatları, 1:25, 1:50 ve 1:100 oranlarında S. aureus ile enfekte edilmiştir. Hücre içi enfeksiyon Giemsa boyama ile görselleştirilmiş, CFU analizi ile bakteriyel yük belirlenmiş, enfeksiyon indeksi hesaplanmıştır. Hücre döngüsü ve apoptoz analizi, akış sitometrisi ile gerçekleştirilmiş, DNA hasarını incelemek için immünofloresan boyama yapılmıştır. Kanser hücrelerinin metastatik potansiyelini değerlendirmek amacıyla koloni oluşum ve migrasyon testleri uygulanmıştır. CD44 ve CD133 kanser kök hücre belirteçlerinin ifadesi incelenmiştir. Kanser progresyonu, apoptoz ve hücre göçü ile ilişkili genlerin ekspresyon düzeyleri RT-PCR yöntemiyle analiz edilmiştir.

Sonuçlar: Elde edilen veriler, S. aureus enfeksiyonunun A549 ve BEAS-2B hücre hatlarında farklı oranlarda belirgin değişikliklere neden olduğunu göstermiştir. Özellikle A549 hücrelerinde apoptoz, hücre döngüsü, DNA hasarı ve metastatik/kök hücre benzeri özellikler üzerinde etkili olduğu gözlemlenmiştir. Ayrıca, enfeksiyonun kanser progresyonu, apoptoz ve hücre göçü ile ilişkili genlerin ekspresyonunu değiştirdiği belirlenmiştir.

Tartışma: Elde edilen bulgular, S. aureus'un akciğer hücreleriyle etkileşimine dair moleküler düzeyde önemli bilgiler sunmakta ve bakteriyel enfeksiyonların kanser biyolojisi üzerindeki etkilerine ışık tutmaktadır. Bakteriyel enfeksiyonların kanser progresyonu ve tedavisindeki rolüne yönelik daha ileri fonksiyonel çalışmaların yapılması gerekmektedir.

Anahtar Kelimeler: Staphylococcus aureus, bronchial epithelial cell, cancer cells, cancer stem cell, infection

Poster Presentation – 42

The Impact of Scorpion Venom on Autophagy: A Double-Edged Sword in Cancer Therapy

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Scorpion venom, composed of diverse bioactive peptides and enzymes, has emerged as a potential modulator of autophagy in cancer treatment. Autophagy plays a paradoxical role in cancer, acting as a tumor suppressor by maintaining cellular homeostasis in early stages, while promoting tumor survival and therapy resistance in advanced stages. Understanding how scorpion venom influences autophagy could offer novel therapeutic strategies tailored to different cancer stages. Scorpio fuscus venom at 10 µg/mL induces a 2.5-fold increase in LC3-II levels in U87 glioma cells, signifying enhanced autophagosome formation. Concurrently, p62/SQSTM1 levels decreased by 40%, confirming active autophagic flux. In MCF-7 breast cancer cells, venom exposure elevated Beclin-1 expression by 1.8-fold, resulting in a 35% reduction in cell proliferation over 48 hours. Interestingly, co-treatment with scorpion venom and chloroquine, an autophagy inhibitor, led to a synergistic 60% decrease in tumor cell viability, suggesting that venom-induced autophagy sensitizes cancer cells to therapeutic agents. Mechanistic insights indicate that venom peptides inhibit the PI3K/Akt/mTOR pathway, a key regulator of autophagy, thereby inducing autophagy. These findings highlight the double-edged nature of autophagy in cancer-scorpion venom may promote cancer cell death in early stages by inducing autophagy but could support tumor survival in later stages. Therefore, precise modulation of venom-induced autophagy represents a promising approach to overcome drug resistance and optimize cancer therapy.

Poster Presentation – 43

Differential cross-talk of *Staphylococcus epidermidis* in a co-culture model of lung cancer and bronchial epithelial cells

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Staphylococcus epidermidis, a common opportunistic pathogen, plays a significant role in respiratory infections, especially in cancer patients. The interaction between airway epithelial cells and pathogens is crucial for understanding host-pathogen dynamics. This study aimed to investigate the effects of S. epidermidis on lung cancer (A549) and healthy bronchial epithelium cells (BEAS-2B) by co-culture.

Material and Methods: A549 and BEAS-2B cells were co-cultured and subsequently infected with S. epidermidis at 1:50 and 1:100 ratios for 4 hours. The infection index was calculated to evaluate the bacterial adhesion and invasion capacity. Giemsa staining was performed to visualize bacterial attachment and intracellular localization. Total RNA was extracted from infected and control cells, and RT-PCR analysis was conducted to assess the impact of infection on the expression levels of cancer-related genes. Cell cycle and apoptosis assays were quantitatively analyzed by flow cytometry. Migration assays were conducted to evaluate the metastatic capacities of the infected cells.

Results: The findings of this study revealed significant changes in the A549 and BEAS-2B cell lines infected with S. epidermidis at different rates. New information on the possible influence of bacterial infection on cancer biology was revealed by changes in gene expression linked to the advancement of cancer. Molecular mechanisms by which S. epidermidis interacts with normal bronchial epithelial cells as well as lung cancer cells have been identified.

Discussion: These findings suggest that interactions between alveolar and bronchial epithelial cells influence bacterial invasion and persistence. Further investigation of the effects of S. epidermidis on cancer cells will help to elucidate epithelial susceptibility to this bacterium and the mechanisms of cancer development.

Poster Presentation – 44

Effect of different serum concentrations on breast cancer cells infected with *Staphylococcus* spp.

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Introduction and Aim: Breast cancer cells exhibit remarkable adaptability to metabolic stress, a key factor in tumor progression and treatment resistance. Starvation is a complex phenomenon that enables tumor survival and progression through various molecular mechanisms and signaling pathways. Recent studies have identified Staphylococcus spp. as the most commonly detected bacteria in breast cancer tissue. Understanding the molecular mechanisms underlying breast cancer, as well as clarifying the impacts of both starvation and staphylococcal infection, is crucial for developing effective therapies against this disease.

Material and Methods: We investigated the effects of long-term starvation on MCF-7 breast cancer cells and their response to subsequent bacterial infection. MCF-7 cells were cultured under serum-deprivation conditions containing 1%, 10%, and 20% FBS for one month to induce metabolic stress. Subsequently, the cells were infected with Staphylococcus epidermidis and S. aureus at infection ratios of 1:50 and 1:100. To evaluate the effects of infection and metabolic stress, migration assays were performed to assess cell motility. Giemsa staining was used to visualize intracellular infection. Colony-forming unit analysis was conducted to quantify the intracellular bacterial load, and the infection index was calculated. Cell cycle and apoptosis assays were conducted using flow cytometry. RNA isolation was performed using the TRIzol method, followed by gene expression analysis to investigate the molecular responses to prolonged starvation and infection.

Results and Discussion: Our findings suggest that serum-related metabolic stress significantly affects the response of breast cancer cells to Staphylococcus infection. Gene expression changes and cell death analyses show that altered serum concentrations reduce the resistance of cancer cells to Staphylococcus infection and significantly increase cell death. In conclusion, our study provides valuable insights into the axis of serum-related metabolic stress, breast cancer progression, and Staphylococcus infection. This underscores the importance of metabolic conditions in influencing tumor behavior and resilience against infections.

Poster Presentation – 45

Resveratrol Enhances the Antiproliferative Effect of GLUT-1 Inhibition in Lung Cancer Models

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Introduction and Aim: Lung cancer remains one of the leading causes of cancer-related mortality worldwide, largely due to late-stage diagnosis and limited treatment efficacy. A key hallmark of tumor progression is metabolic reprogramming, including enhanced glucose uptake to sustain rapid proliferation. Glucose transporter 1 (GLUT-1), frequently overexpressed in lung cancer, plays a central role in this metabolic shift and has been associated with poor prognosis. Targeting GLUT-1-mediated glucose transport represents a promising therapeutic strategy. Resveratrol, a polyphenolic compound found in red fruits, possesses antioxidant, anti-inflammatory, and antiproliferative properties. Due to its structural similarity to tyrosine kinase inhibitors, Resveratrol has been proposed to modulate GLUT-1 activity and impair glucose metabolism in cancer cells. This study aimed to investigate the combined effect of GLUT-1 inhibition and Resveratrol on the viability and proliferation of lung cancer cells.

Materials and Methods: Human A549 and murine Lewis Lung Carcinoma (LLC-1) cell lines were used as models. Cells were treated in four groups: control (DMSO), GLUT-1 inhibitor, Resveratrol, and the combination of both agents. Viability was assessed using the Sulforhodamine B (SRB) assay. Synergistic interactions were evaluated via combination index (CI) analysis. The most effective dose combination was further assessed with time-dependent viability and colony formation assays.

Results: Combined treatment with GLUT-1 inhibitor and Resveratrol led to a significant synergistic reduction in cell viability in both cell lines. The combination of 6 μM Resveratrol and 20 μM GLUT-1 inhibitor yielded the strongest effect, with a CI of 0.59, indicating marked synergism. Growth inhibition increased up to 5.5-fold compared to single-agent treatments.

Discussion: These findings suggest that concurrent inhibition of GLUT-1 and Resveratrol treatment exerts a synergistic antitumor effect in lung cancer cells, supporting its potential as a novel therapeutic strategy.

Key words: Lung cancer, GLUT-1 inhibition, Resveratrol, Metabolic reprogramming, Synergistic therapy

Poster Presentation – 46

GST Activities of *Ornithogalum sigmoideum* on HEPG2 Hepatocellular Carcinoma and HT-29 Colon Cancer Cell Lines

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Introduction and Aim: *Ornithogalum* L. is a genus comprising approximately 200 species distributed across warm regions of Europe, Asia, and Africa, 54 of which grow naturally in Turkiye. The aerial parts and bulbs of *Ornithogalum* species are consumed as food and have been employed in ethnomedicine for various therapeutic purposes worldwide. Notably, *Ornithogalum sigmoideum*, which is commonly consumed in the Black Sea Region, has been reported to significant anti-inflammatory and antioxidant capacity and is particularly rich in phenolic and flavonoid compounds. In light of these health-promoting effects; we aimed to study glutathione -S-transferase (GST) activities of aerial parts and bulbs of *Ornithogalum sigmoideum* in HEPG2 human hepatocellular cancer and HT-29 human colon cancer cell lines.

Materials and Methods: The cytotoxic effects were evaluated on colorectal (HT-29) and hepatocellular (HEPG2) cancer cells using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The glutathione -S-transferase activity was determined using 1-chloro-2,4-dinitrobenzene (CDNB) and 1,2-epoxy-3-(p-nitrophenoxy) propane (EPNP) as GST substrates.

Results: In the HEPG2 hepatocellular carcinoma cell line, Ornitagalum underground extract statistically significantly reduced total GST activity. Ornitagalum underground extract reduced total GST activity %48,27 compared to the control group ($p < 0,001$). Ornitagalum underground extract statistically significantly increased total GST specific activity in HT-29 colon cancer cell line ($p < 0,001$).This increase rate was calculated as %44,99.

Discussion: Reducing the total GST activity of cancer cells may bring about medically important advantages such as both the death of these cells and the reduction/elimination of their resistance to chemotherapeutic agents. Therefore, the use of GST inhibitors or other methods to reduce GST activity is becoming increasingly important in studies aimed at developing current cancer treatment strategies.

Key words: Glutathione-S-transferase, *Ornithogalum sigmoideum*, HEPG2, hepatocellular carcinoma, HT-29, colon cancer.

Poster Presentation – 47

Immunomodulatory Effects of Walnut Husk Extract on LPS-Stimulated RAW 264.7 Cells and Its Cytotoxic Impact on K7M2 Osteosarcoma Cells

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Introduction and Aim: Osteosarcoma is the most common primary malignant bone tumor in children and young adults, characterized by its aggressive nature and high metastatic potential. Current treatment options are limited and can cause severe side effects. Tumor-associated inflammation plays a key role in osteosarcoma progression. The walnut husk, the greenish outer covering of the walnut fruit, is rich in polyphenols and phytochemicals. This study aimed to investigate the immunomodulatory effects of walnut husk extract (WHE) on LPS-stimulated RAW 264.7 macrophages and its indirect impact on K7M2 osteosarcoma cell viability.

Materials and Methods: WHE was prepared from fresh and dried husks. The husks were chopped, extracted with 80% methanol in an ultrasonic bath for 1 hour, and subjected to rotary evaporation and lyophilization. The total phenolic content (TPC), flavonoid content (TFC), and antioxidant capacity (TAC) were measured spectrophotometrically. RAW264.7 macrophages were stimulated with LPS(1µg/mL) and treated with WHE at concentrations of 10–1000 µg/mL for 24 hours. The supernatants were then applied to K7M2 osteosarcoma cells for 24 hours, and cell viability was assessed using the WST-1 assay.

Results: WHE exhibited high TPC (33.33mgGAE/g), TFC (9.77mgQE/g), and TAC (68.69% inhibition). No cytotoxic effect was observed on RAW264.7 macrophages. When applied to K7M2 cells, WHE significantly reduced cell viability starting at 250 µg/mL($p < 0.05$). The reduction was more pronounced when K7M2 cells were exposed to supernatants from LPS-stimulated RAW264.7 cells treated with WHE, with significant decreases at ≥50 µg/mL($p < 0.05$), indicating an immunomodulatory effect.

Discussion: These results demonstrate that WHE has both direct and indirect cytotoxic effects on osteosarcoma cells. Its non-toxic profile toward macrophages and ability to modulate inflammation suggest WHE as a promising compound for targeting the osteosarcoma tumor microenvironment. Further studies are needed to explore its molecular mechanisms and validate these results in *in vivo* models.

Key words: Osteosarcoma, walnut husk extract, RAW264.7 macrofages, immunomodulation.

Poster Presentation – 48

Dual Impact of a Herbal Oil Combination on SARS-CoV-2 Entry Pathways and Tumorigenic Signaling in Colon Adenocarcinoma Cells

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Introduction and Aim: SARS-CoV-2 enters host cells via ACE2, TMPRSS2, and Furin, molecules also implicated in tumorigenesis, particularly in epithelial cancers [1]. This study explores the antiviral and potential anticancer properties of a novel herbal oil combination by evaluating its effects on these targets in HT-29 colon adenocarcinoma cells.

Materials and Methods: HT-29 cells were treated with increasing concentrations (0.75–60 µg/ml) of the herbal oil combination. Cell viability was assessed via ATP assay (Promega, USA). Protein expression levels of ACE2, TMPRSS2, and Furin were analyzed through Western blotting and ELISA at the highest non-toxic concentration (0.75 µg/ml).

Results: Cell viability was assessed using ATP assays determining 0.75 µg/ml as the highest non-toxic dose. Western blot and ELISA analyses demonstrated a significant downregulation of ACE2, TMPRSS2, and Furin protein levels upon treatment at this concentration ($p < 0.05$ to $p < 0.001$). Quantitatively, ACE2 expression was reduced by ~25%, TMPRSS2 by ~50%, and Furin by ~20–30%. Higher concentrations (>1.5 µg/ml) induced a dose-dependent cytotoxic response.

Discussion: Given the dual role of these proteins in both viral entry and cancer progression (e.g., epithelial-mesenchymal transition, invasion, and tumor microenvironment modulation), these findings suggest that the herbal combination may serve as a promising candidate not only against COVID-19 but also as a supportive agent targeting oncogenic signaling pathways.

Key words: Cancer, Colon, ACE2, TMPRSS2, Furin, herbal oil combination.

References

1. Tanrıverdi, Ö., Alkan, A., Karaoglu, T., Kitaplı, S. & Yildiz, A. COVID-19 and Carcinogenesis: Exploring the Hidden Links. *Cureus* 16, e68303, doi:10.7759/cureus.68303 (2024).

Glioblastoma Hücrelerinin Anjiyogenezinde Etkin Rol Oynadığı Bilinen VEGFR Sinyal Yolağı, Yeni Bir İnhibitör Olan Donafenib ile Baskılanabilir Mi?

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Giriş ve Amaç: Dünya Sağlık Örgütü tarafından derece 4 astrositom olarak sınıflandırılan Glioblastoma Multiforme (GBM), merkezi sinir sisteminde görülen en agresif beyin tümörüdür. DNA alkilleyici bir kemoterapötik olan Temozolomid (TMZ), GBM hastalarına birinci basamak tedavi olarak uygulanmaktadır. Donafenib (DNF) ise VEGFR, PDGFR ve çeşitli Raf kinazların aktivasyonunu inhibe eden küçük moleküllü yeni bir multikinaz inhibitörüdür. Bu inhibisyonu sayesinde tümör hücre proliferasyonu ve anjiyogenezini baskıladığı bilinmektedir. Tüm bu bilgiler ışığında çalışmamız; "GBM hücre anjiyogenezinde rol oynadığı bilinen VEGFR2 protein düzeyinin; DNF'in bireysel ve TMZ ile kombine uygulamasıyla azabileceği" hipotezinden yola çıkarak kurgulanmıştır. Amacımız; daha önce GBM'de hiç çalışılmamış bu inhibitörün tümör hücre proliferasyonu ve anjiyogenezinde etkin olduğu bilinen yolaklardaki değişimini *in vitro* olarak değerlendirmektir.

Materyal ve Metot: Çalışmamızda hem TMZ duyarlı U87MG hem de TMZ dirençli T98G hücre hatları kullanıldı. Deneysel gruplarımız; Kontrol, Çözücü (DMSO), TMZ, DNF ve TMZ+DNF uygulamalarını içermektedir. TMZ ve DNF'nin GBM hücrelerine hem bireysel hem de kombine uygulanmasıyla hücre proliferasyon ve anjiyogenezinden sorumlu sinyal yolu protein düzeyleri (p-STAT3, STAT3, p-VEGFR2, VEGFR2 ve NF-κB) immünositokimyasal analiz ile değerlendirildi.

Bulgular: GBM hücrelerine DNF'nin hem bireysel hem de TMZ ile kombine uygulanmasıyla tümör hücre proliferasyonunda rol alan STAT3, p-STAT3 ve NF-κB protein düzeylerinin kontrol grubuna göre hem hücre sayısına hem de protein yoğunluğuna bağlı azaldığı gösterildi. Buna ilaveten, GBM hücrelerinde bu uygulamalar sonrası anjiyogenez belirteci olan VEGFR2 ve p-VEGFR2 protein yoğunluklarının kontrol grubuna kıyasla anlamlı düzeyde azaldığı görüldü. U87MG hücrelerinin yanı sıra özellikle TMZ'ye dirençli olan T98G hücrelerinde DNF'nin bu denli etkin olması son derece dikkat çekiciydi.

Tartışma: Çalışmamızla, tümör hücre proliferasyonu ve anjiyogenezinde rol oynayan sinyal yolu protein düzeylerinin TMZ ve DNF uygulamasıyla azaldığı gösterildi. Literatürde, TMZ'nin GBM hücre proliferasyonuna olan etkisi bilinmesine rağmen DNF'nin GBM hücrelerinde henüz çalışılmadığı dikkat çekmektedir. Bu nedenle, elde ettiğimiz bulgular literatürdeki bu açığı kapatarak; yeni çalışmaların kurgulanması için önemli katkılar sunabileceği kanaatindeyiz.

Anahtar Kelimeler: Glioblastoma Multiforme, Temozolomid, Donafenib

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Poster Presentation – 50

Investigation of the Synergistic Effect of Quercetin and Epigallocatechin Gallate on Doxorubicin in Triple Negative Breast Cancer Cell Lines

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Introduction and Aim: Triple-negative breast cancer (TNBC) is an extremely aggressive subtype with high recurrence and mortality rates, which is especially observed in young women under the age of 45. TNBC is characterized by the absence of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor (HER2) expression, thereby lacking a targeted treatment approach. Therefore, conventional chemotherapy agents such as doxorubicin, which has severe adverse effects, are often used in TNBC treatment. Another challenges in TNBC treatment are intratumoral heterogeneity, treatment resistance, and tumors' ability to alter signalling pathways to survive. Since polyphenolic compounds have an impact on a wide range of pathways without showing any side effects, this study aims to investigate the effect of a dual phytochemical mixture (Quercetin and Epigallocatechin-3-Gallate (EGCG)) with anti-cancer features on Doxorubicin to achieve maximum benefit with minimum side effects and its effects on cell viability.

Materials and Methods: In this study, Doxorubicin, EGCG and Quercetin were applied at different doses and times to the MDA-MB-231 cell line modeling TNBC. Based on their cytotoxic effects, a mixture was formed. MTT was performed to detect cytotoxicity. For statistical analyses, a two-way anova test was applied using GraphPad Prism 10. P values less than 0.05 were considered significant.

Results: Significant cytotoxic effects of the mixture were observed starting from 40% dose at the 48th hour and from 25% dose at the late stage at the 72nd hour.

Discussion: As a result of MTT analysis, the synergistic effect of Quercetin and EGCG showed a more significant cytotoxic effect on doxorubicin.

Key words: Polyphenolic compounds, breast cancer, cytotoxicit

Poster Presentation – 51

Green Synthesis of Zinc Oxide Nanoparticles (Znonps) And Investigation of Their Cytotoxic Effects On Colorectal Carcinoma Cells

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The rapid development of nanotechnology has increased the use of nanomaterials in the biomedical field. Nanoparticles, particularly zinc and zinc oxide nanoparticles (ZnONPs), attract attention as trace elements involved in essential biological functions in the human body [1]. Colorectal cancer is one of the leading fatal diseases occurring in the final part of the large intestine [2]. Current cancer treatment methods are often problematic due to their high costs and side effects. Therefore, searching for new and more effective treatment methods is very important. The study aims to investigate the effects of ZnONPs on the hCRC cell line. The results obtained from the study aim to explain the impact of zinc oxide nanoparticles in cancer therapy while providing a new perspective on the increasing use of nanoparticles in the biomedical field. The green synthesis of zinc oxide nanoparticles using tannic acid was performed, and the characterization of the synthesized nanoparticles was accomplished using UV-Vis spectroscopy, dynamic light scattering (DLS), Fourier transform infrared spectroscopy (FT-IR), and scanning electron microscopy (SEM). The cell viability and cytotoxicity analysis of the synthesized zinc oxide nanoparticles was done using the Alamar Blue assay. The IC_{50} value was determined using a sigmoidal plot of inhibition vs. a log of ZnONP concentration. UV-vis spectroscopy results proved the synthesis of one type of ZnONPs, which gives a maximum absorbance at 350 nm. SEM and DLD analyses of ZnONPS demonstrated that the particle size was measured as 35 nm following the green synthesis of particles. The synthesized ZnO nanoparticles exhibited a dose-dependent cytotoxic effect on DLD-1 cells, with an IC_{50} value of 12.4 µg/mL. These results suggest that ZnO nanoparticles synthesized with tannic acid could be a promising therapeutic agent for colorectal cancer treatment. The findings may help create new approaches for cancer therapy. These findings highlight the potential of ZnO nanoparticles as promising anticancer agents, offering an eco-friendly and cost-effective alternative for nanomedicine applications.

Key words: Zinc Oxide Nanoparticle, Green Synthesis, Colorectal Carcinoma, Cytotoxicity

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Reference:

1. Labianca, R., et al., *Colon cancer.* Critical reviews in oncology/hematology, 2010. 74(2): p. 106-133.

2. Wiesmann, N., et al., *Zinc overload mediated by zinc oxide nanoparticles as innovative anti-tumor agent.* Journal of Trace Elements in Medicine and Biology, 2019. 51: p. 226-234.

Poster Presentation – 53

Re-Evaluation of Personally Appropriate Therapeutic Approaches in Patients Diagnosed with Small Cell Lung Cancer Wth Liquid Biopsy and Clinical Data Integration

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Lung cancer is one of the most commonly diagnosed cancers worldwide and a leading cause of cancer-related deaths. Small cell lung cancer (SCLC) accounts for approximately 15% of all lung cancers diagnosed worldwide and 25% of lung cancer deaths (Mondelo-Macía et.al.2021). The detection of circulating biomarkers is a practical approach for the early diagnosis of lung cancer. In order to apply the most appropriate therapeutic strategy for each patient, it is still necessary to identify new predictive biomarkers that will lead to a better understanding of its molecular mechanisms (Church et al.2020). A more detailed understanding of the molecular mechanisms is needed to improve personalized therapeutic approaches in SCLC along with enabling the discovery of effective biomarkers for predictive purposes. For this particular purpose, the liquid biopsy approach could be used (Russano et al. 2020). This study will attempt to answer the question of whether a more appropriate therapeutic strategy for SCLC can be developed by integrating the molecular knowledge gained with the clinical information, treatment protocols of patients. After the enrollment of 40 patients diagnosed with SCLC, the isolation of cfDNA will be performed and it will be followed by the liquid biopsy performed with QIAGENE NGS panel in which 63 genes will be checked. Then, the results of this panel will be correlated with the treatment response of SCLC patients to capture any personal signatures as part of the treatment response.

Keywords: Small Cell Lung Cancer; Liquid Biopsy; Personalized Treatment in Oncology

References:

1. Mondelo-Macía, P., García-González, J., León-Mateos, L., Castillo-García, A., López-López, R., Muinelo-Romay, L and Díaz-Peña, R. 2021. “Current Status and Future Perspectives of Liquid Biopsy in Small Cell Lung Cancer”, Biomedicines, 9, 48.

2. Church, M., Carter, L., and Blackhall, F. 2020. “Liquid Biopsy in Small Cell Lung Cancer—A Route to Improved Clinical Care?”, Cells, 9, 2586.

3. Russano, M., Napolitano, A., Ribelli, G., Iuliani, M., Simonetti, S., Citarella, F., Pantano, F., Dell’Aquila, E., Anesi, C., Silvestris, N., et al. 2020. “Liquid biopsy and tumor heterogeneity in metastatic solid tumors: The potentiality of blood samples”, J. Exp. Clin. Cancer Res., 39, 120.

Poster Presentation – 54

May The Newly Identified Interleukins Be Considered as A New Potential Therapeutic Target in The Treatment of Breast Cancer?

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Background/aim: Breast cancer, which is the most common malignant tumor among women worldwide. The function of newly defined intrelekins remains unclear and whether interleukin levels impact breast cancer risk or outcome is unknown (1,2). This work focused on what is the role and the involvement of newly defined interleukins in breast cancer before and radiotherapy. The present study's main aim is to understand newly defined interleukins' roles in breast cancer development a specifically during the radiotherapy and identify new therapeutic targets and strategies for breast cancer treatment (3,4).

Materials and methods: Twenty-five women with breast cancer enrolled in the study. Blood samples were taken before and after radiotherapy, interleukins 35, 39, 40 and 41 levels were determined with ELISA kits.

Results: Although there was no clear statically difference in levels of IL-35, IL-39, IL-40 and IL-41 before and after radiotherapy, ($p = 0.088$, $p = 0.619$, $p = 0.925$ and $p = 0.122$ respectively), IL-35 and IL-40 levels were seem to clearly increased numerically after radiotherapy, whereas IL-39 and IL-41 levels in a similar sense clearly decerased numerically also again after radiotherapy. In addition there was different correlations degrees observed between interlekins levels.

Conclusion: This study aimed to evaluate the newly identified interleukins in breast cancer patients who underwent radiotherapy and shed light on this with a limited number of patients. Not statistical but the numerical changes obtained with this study indicate that IL-35, IL-39, IL-40 and IL-41 are closely related to tumor development and can be used in breast cancer clinical research and treatment. Therefore, this study will aid in the development of breast cancer immunotherapy regimens based on interleukins and will also help whether guide their use as more effective and safe immunotherapy tools with the use of larger number samples.

Key words: Breast cancer, IL-35, IL-39, IL-40, IL-41 and radiotherapy

References

1- Advances in Radiotherapy for Breast Cancer, Upadhyay R, Bazan JG.Surg Oncol Clin N Am. 2023 Jul;32(3):515-536. doi: 10.1016/j.soc.2023.03.002.

2- Updates in the Treatment of Breast Cancer with Radiotherapy, Castaneda SA, Strasser J.Surg Oncol Clin N Am. 2017 Jul;26(3):371-382. doi: 10.1016/j.soc.2017.01.013. Epub 2017 May 11.

3-Cytokine Modulation in Breast Cancer Patients Undergoing Radiotherapy: A Revision of the Most Recent Studies, Marconi R, Serafini A, Giovanetti A, Bartoleschi C, Pardini MC, Bossi G, Strigari L.Int J Mol Sci. 2019 Jan 17;20(2):382. doi: 10.3390/ijms20020382.

4-Predicting Response to Radiotherapy in Cancer-Induced Bone Pain: Cytokines as a Potential Biomarker? MacLeod K, Laird BJA, Carragher NO, Hoskin P, Fallon MT, Sande TA.Clin Oncol (R Coll Radiol). 2020 Oct;32(10):e203-e208. doi: 10.1016/j.clon.2020.03.010. Epub 2020 Apr 11.

Poster Presentation – 55

Importazole as a novel inhibitor of ARF6: Inhibits the growth of colon cells and induces apoptosis

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Introduction and Objectives: Colorectal cancer (CRC) is a leading cause of cancer-related mortality. Importin β1 regulates the cell cycle, while ADP-ribosylation factor 6 (ARF6) promotes metastasis via plasma membrane protein endocytosis. This study examines the effects of Importazole, an Importin β1 inhibitor, on CRC cell viability, colony formation, ARF6 expression, and apoptotic gene regulation. Additionally, ARF6's role in CRC pathogenesis was analyzed using bioinformatics approaches.

Materials and Methods: Clinical RNA-seq data for colon adenocarcinoma (COAD) from The Cancer Genome Atlas (TCGA) were analyzed to identify differentially expressed genes (DEGs). Pathway enrichment was performed using ConsensusPathDB, which integrates KEGG and Reactome databases. A protein-protein interaction (PPI) network was constructed using the BioGRID dataset and visualized with Cytoscape, identifying ARF6 as a major hub protein. ARF6 expression across malignancies was assessed via GEPIA2 and the Human Protein Atlas. Drug repurposing analysis was performed using DrugGeneBudger. HT-29 cells were treated with Importazole and cell viability and colony formation were evaluated. qRT-PCR analyzed the expression of ARF6, BCL2, BAX, CASPASE3, and TP53.

Results: A total of 2,022 DEGs were identified, and ARF6 emerged as a significant hub protein. Bioinformatics analysis confirmed ARF6 overexpression in CRC compared to normal tissues. Importazole treatment significantly reduced HT-29 cell viability in a dose-dependent manner, with an IC50 of 68.06 μM, and 10 μM Importazole effectively inhibited colony formation. qRT-PCR analysis showed Importazole downregulated ARF6 expression while upregulating the BAX/BCL2 ratio and CASPASE3, indicating apoptosis induction.

Discussion: Importazole suppressed CRC cell survival and colony formation while inducing apoptosis via ARF6 downregulation. The changes in apoptotic gene expression suggest Importin β1 inhibition affects ARF6-mediated oncogenic pathways. Bioinformatics analysis highlights ARF6 as a potential CRC therapeutic target. These findings suggest Importazole as a promising candidate for CRC treatment.

Key words: Colorectal cancer, Importin β1, Importazole, ARF6, apoptosis.

Poster Presentation – 56

Novel Heteroleptic Iridium (III) Complex for Bioimaging of Lung Cancer Cells

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Bioimaging has become a crucial and adaptable tool in biomedical research, allowing scientists to visualize and track biological processes at the cellular and molecular scales. Transition metal complexes, especially those with d^6 electronic configurations, have attracted considerable interest for their applications in bioimaging [1,2]. Among iridium (III) complexes, both homoleptic and heteroleptic cyclometallated variants have shown great promise in bioimaging applications thanks to their intense and tunable phosphorescence emission [3].

In this study, a new heteroleptic iridium (III) complex was synthesized using 2-(4-trifluoromethylphenyl) pyridine as a C^N-type ligand and methacryloyltyrosine (MATyr) an L^X-type ligand. Then, the synthesized Ir (III) complex was conjugated with transferrin protein through microemulsion polymerization technique [4]. Iridium-transferrin cross-linked conjugates were used as bioimaging markers for A549 (ATCC®CCL-185TM) cells.

The interaction between the Ir-Tf complex and transferrin receptors on the surface of cancer cells induced fluorescence, allowing for precise visualization of the cancer cells. This study marks a significant advancement in bioinorganic chemistry. The development of Ir-Tf conjugate introduces a new class of biomaterials with promising applications in bioimaging.

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Key words: Ir (III) complex, microemulsion, bioimaging, lung cancer cells.

References

[1] R.J. Watts, J. Van Houten, J. Am. Chem. Soc. 96 (1974) 4334-4335. https://doi.org/10.1021/ja00820a053

[2] Y. You, *Curr Opin* Chem Biol. 17 (2013) 699–707. http://dx.doi.org/10.1016/j.cbpa.2013.05.023.

[3] A. Zamora, G. Vigueras, V. Rodríguez, M. D. Santana, J. Ruiz, Coord. Chem. Rev., 360 (2018) 34-76. https://doi.org/10.1016/j.ccr.2018.01.010.

[4] Ö.B. Ünlüer, Ö. Tomsuk, A. Ersöz, H. Sivas, R. Say. Biotechnol. Prog. 29 (2013) 472-479. https://doi.org/10.1002/btpr.1674.

Integration of Bacterial and Eukaryotic Microbiota and Lipidomics Data in Consecutive Saliva and Fecal Samples of Lung Cancer

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Introduction: Microbiota-targeted biomarkers are emerging as promising noninvasive tools for the early detection of cancers. Increasing evidence suggests that alterations in microbiota can lead to significant disruptions in lipid metabolism. This study aims to investigate the oral and intestinal microbiome, lipidome, and their interactions, which hold substantial potential for providing clinical guidance.

Material and method: To achieve this, lipid profiles, as well as prokaryotic and eukaryotic microorganisms, were determined by collecting consecutive stool and saliva samples from lung cancer (LC) patients and healthy controls (HC) at three time points: pre-treatment, and at 6- and 12-months post-treatment. In all these samples, the 16S rRNA and 18S rRNA genes for bacteria and eukaryotes, respectively, were sequenced with an oxford nanopore platform. Lipid profile was investigated using nanoflow ultra-high performance liquid chromatography-electrospray ionization-tandem mass spectrometry. All data were evaluated and integrated by bioinformatics analysis.

Result and discussion:18S rRNA analyses indicated that stool samples from LC patients had significantly higher evenness and diversity, with comparable OTU counts to HC. Saliva samples from LC patients showed a higher OTU count but similar evenness and diversity. In contrast, 16S rRNA analysis revealed lower OTU counts in both stool and saliva samples from LC patients compared to HC; however, OTU counts increased over time in consecutive samples from LC patients. Beta-diversity analysis showed no significant differences in microbiota composition between HC and LC patients, although initial and second samples from LC patients exhibited similar clustering patterns. 18S rRNA analyses revealed that Ascomycota was less abundant, while Mucoromycota was more abundant in the saliva of LC patients compared to HC; the opposite was true for stool samples.

Pichia kudriavzevii was less abundant, while Carcinomyces was more abundant in saliva samples from LC patients. 16S rRNA analyses showed that Firmicutes were significantly more abundant in both samples from LC patients, while Euryarchaeota were less abundant in saliva. Streptococcus and

Blautia were more abundant in both samples of LC patients, respectively, while Levilactobacillus was more abundant in stool from HC. Lipidomic analysis revealed increased diacylglycerol levels in saliva, potentially due to bacterial stimulation. Ceramide in LC patients correlated positively with Firmicutes, a correlation not seen in HC. Phosphatidylserine, found in saliva, may serve as a biomarker for LC, with significantly reduced levels in LC patients and a correlation with gram-negative bacteria.

Conclusion: This study demonstrates that microbiota may play critical roles in cancer development through their impact on lipid metabolism; however, further research is needed to explore this relationship in greater depth (supported by TUBITAK-120N924).

Key Words: Lung cancer, Microbiota, Lipidomics, 16S rRNA

Pankreas Kanseri Araştırmalarında İdeal 3D Sferoid Modellerin Belirlenmesi: Agaroz ve GelMA'nın Karşılaştırılması

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Giriş ve Amaç*:* Pankreas kanseri, klinik olarak yüksek mortalite oranlarıyla seyreden ve tedaviye direnç gösteren agresif bir kanser türüdür. Geleneksel iki boyutlu (2D) hücre kültür sistemleri, kanser hücrelerinin mikro çevresiyle etkileşimlerini gerçekçi biçimde yansıtamamaktadır. Tümör mikro ortamını daha doğru şekilde taklit edebilen üç boyutlu (3D) hücre kültürleri, 2D hücre kültürüne nazaran çok tabakalı heterojen bir yapı oluşturan, hayvan deneyleri ile 2D hücre kültürü çalışmaları arasındaki boşluğu dolduran bir *in vitro* çalışma alanıdır. Bu çalışmanın amacı, pankreas kanseri araştırmalarında kullanılmak üzere en uygun biyomalzeme tabanlı 3D sferoid modelinin belirlenmesidir.

Gereç ve Yöntemler: Bu çalışmada, PANC-1 ve MIA PaCa-2 pankreas kanseri hücre hatlarında agaroz (%3) ve jelatin metakrilat (GelMA, %10) bazlı biyomalzemeler kullanılarak oluşturulan sferoidlerin morfolojik yapısı değerlendirilmiş; hücre süspansiyonu ve asılı damla gibi farklı yöntemlerle hazırlanan sferoidlerin stabiliteleri karşılaştırılmıştır. Sferoidlerin 24, 48 ve 72. saatteki yapılarının fotoğrafları çekilerek Image J programı ile boyutları ölçülmüştür.

Sonuçlar: PANC-1 hücrelerinde GelMA'ya aktarılan asılı damla sferoidleri bütünlüğünü korurken, hücre süspansiyonunun GelMA'ya eklenmesiyle sferoid oluşmadığı görülmüştür. MIA PaCa-2 hücrelerinde ise GelMA'ya transfer edilen asılı damla sferoidlerinin dağıldığı, hücre süspansiyonunun eklenmesi sonucunda da sferoid oluşmadığı belirlenmiştir. Her iki hücre hattında hücre süspansiyonlarının agaroza eklenmesinin ardından 24. saatte sferoid oluşumu gözlenmiş; üstelik asılı damla yöntemi ile aktarılan sferoidlerin küresel yapılarının 72. saate kadar bozulmadan kaldığı görülmüştür. Yapılan incelemelerde hem PANC-1 hem de MIA PaCa-2 hücre hattında en iyi sonuç, asılı damla yöntemiyle oluşturulan sferoidlerin %3'lük agaroza transfer edildiği gruplarda tespit edilmiştir.

Tartışma: Bu çalışma, agaroz tabanlı biyomalzemelerin pankreas kanseri sferoid modelleri oluşturmak için daha etkili olduğunu ortaya koymuştur. Bu modelin, gelecekte tümör mikroçevresinin simülasyonu, ilaç testleri, metastaz ve anjiyogenez gibi kanser araştırmalarında kullanılması, pankreas kanseri için tedavi ve teşhis yöntemlerinin geliştirilmesine katkıda bulunacaktır.

Anahtar Kelimeler: Pankreas kanseri, biyomalzeme, sferoid, 3D hücre kültürü, doku mühendisliği

Poster Presentation – 59

CRISPR Base Editing Mediated Fluorescent Signal Disruption on Monogenic HEK293T Cells

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Introduction and Aim: The development of genome editing technologies has revolutionized life sciences as it carries the potential to unlock novel treatments of genetic diseases. Of these technologies, base editors can mediate A>G or C>T substitutions on targeted locations which could potentially eliminate most pathogenic point mutations. Apart from their therapeutic applications, adenine and cytosine base editors can also be used to induce mutations on target genes to perform functional studies without disrupting endogenous expression. Here, we established Venus fluorescent protein expressing HEK293T single cell clones to disrupt Venus expression through inducing early stop codons and altering the start codon, using cytosine and adenine base editors respectively as a proof of concept. We aim to use this technology to later create functional mutants of our genes of interest.

Materials and Methods: HEK293T cells were transduced with the LeGO-V2 (Addgene #27340) vector to culture three stable single cell clones, namely 3F1, 3D3, and 5B7. After designing three gRNA constructs, two (C1 and C2) for use with cytosine base editing and one (A) to use with adenine base editing, clones were transfected with SpCas9 TadCBEd-V106W (Addgene #193839) and ABE8e(TadA-8e V106W) (Addgene #138495) vectors alongside gRNA carrying phU6-gRNA (Addgene #53188) constructs to perform the desired edits. Transfected populations were analyzed using flow cytometry and enriched with FACS using DsRed transfection control signal for visualization under a fluorescent microscope.

Results: Fluorescent imaging shows loss of Venus signal on both gRNA and base editor transfected cells, most intensely on the C1 gRNA condition followed by A and C2 respectively. Cells that were transfected with empty gRNA vectors do not show Venus signal loss.

Discussion: These results confirm successful disruption of fluorescence on the developed model system, albeit with low efficiency. Through population enrichment, base editing can be used to establish cell lines expressing mutant proteins for functional studies.

Poster Presentation – 60

Therapeutic Effects of the Antihistamine Desloratadine in Head and Neck Squamous Cell Carcinoma

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Introduction and Purpose: Head and neck squamous cell carcinomas (HNSCC) are tumors with poor prognosis due to treatment resistance and high recurrence rates. Histamine triggers tumor progression by increasing M2 macrophage polarization via H1 receptor and may exert immunosuppressive effects on the tumor microenvironment. Antihistamine drugs may exert antitumor effects by targeting these mechanisms. This study aimed to investigate the effects of the second-generation antihistamine Desloratadine on HNSCC cell lines.

Materials and Methods: UMSCC-47 and HSC-3 cell lines were treated with 20 μM Desloratadine for 48 hours. Cell proliferation, sphere formation, colony formation and capacities were evaluated. Cell cycle distribution was analyzed by flow cytometry. Stem cell-related gene expression levels (KLF4, OCT4, SOX2, NANOG and CD44) were analyzed using RT-qPCR.

Results: Desloratadine treatment caused cell cycle arrest with an increase in G0/G1 phase and a decrease in S phase. A decrease in sphere formation and colony capacities was observed, indicating a decreased ability of tumor cells to self-renew. RT-qPCR analysis revealed significant down-regulation of stem cell-related gene expression.

Discussion: Our findings suggest that desloratadine suppresses proliferation, stem cell-like properties, and self-renewal potential of HNSCC cells. Desloratadine is envisioned to be considered as an adjuvant agent in the treatment of HNSCC, especially in combination strategies. These findings suggest that antihistamine drugs can be repurposed as therapeutic agents targeting the tumor microenvironment.

Key words: Head and Neck Squamous Cell Carcinoma (HNSCC), Desloratadine, Antihistamine, Apoptosis

Poster Presentation – 61

Effects of Biomarkers On Cancer Invasion in Patients with Prostate Cancer

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Background: Identifying reliable biomarkers for prostate cancer remains a critical area of research. Several proteins, including NF-κB, ApoE4, Ang-1, FOXA2, PEN2, and Aβ, have been implicated in various biological processes, but their roles in prostate cancer invasion are not fully understood.

Methods: This study analyzed serum levels of NF-κB, ApoE4, Ang-1, FOXA2, PEN2, and Aβ in blood samples collected from healthy controls, patients with benign prostate hyperplasia, prostate cancer, post-radical prostatectomy patients, and those with metastatic prostate cancer. Enzyme-linked immunosorbent assay (ELISA) methods were used for biomarker quantification.

Results: NF-κB, a key regulator of inflammation and cellular response, showed elevated levels in prostate cancer patients. ApoE4, previously associated with lipid metabolism, was examined for its potential link to prostate cancer risk. Ang-1, a vascular stabilizer, demonstrated relevance to tumor progression. FOXA2, a transcription factor essential in organ development, may contribute to prostate cancer pathogenesis. PEN2, a component of the presenilin complex, was found to be upregulated in prostate cancer cells. Aβ, known for its role in neurodegenerative diseases, was investigated for its potential impact on prostate cancer progression.

Conclusions: While these biomarkers showed varying levels in different patient groups, their clinical utility in prostate cancer diagnosis and prognosis requires further investigation. Additional studies are needed to determine their potential role in cancer invasion and therapeutic applications.

Key words: Prostate cancer, biomarkers, invasion, NF-κB, and FOXA2

A Palladium Complex {[Pd(bpma)(barb)Cl]·H_2O} Triggers Oxidative Stress-Mediated Apoptosis On Ovarian Cancer Cell Lines

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Introduction and Aim: Current chemotherapy treatments for ovarian cancer primarily utilize cisplatin and carboplatin, which are often associated with the development of therapy resistance. Recently, palladium (Pd) complexes have attracted attention due to their higher solubility and less kidney toxicity, compared to platinum analogs. This study focuses on exploring the anti-cancer potential of a palladium complex, [Pd(bpma)(barb)Cl]·H_2O, on ovarian cancer cell lines and uncovering the potential mechanisms involved.

Materials and Methods: SRB and MTT assays were performed on three high-grade serous ovarian cancer cell lines (CaOv-3, Kuramochi, and Ovsaho) at concentrations ranging from 1 nM to 100 μM after 48h treatment. Morphological and biochemical evaluation of cell death modality was performed with fluorescent staining and flow cytometry, respectively. Cellular DNA damage, oxidative stress and cell cyle progression were analyzed with flow cytometry. Cell migration was quantified using the scratch assay (wound healing assay). Gene expression analysis via qPCR was conducted to further characterize the biological response to the treatment.

Results: The Pd complex has cytotoxic and growth inhibitory effect on particularly Ovsaho cells, with 13 μM IC_{50} which was dramatically lower then that of cisplatin. This complex appears to induce apoptosis through mechanisms involving acumulation of ROS that triggers DNA damage which is reversed by sequencial treatment of N- acetylcysteine (NAC). Gene expression profile showed the upregulation of cell cyle related genes *CDC20, CDC25A;* DNA damage related gene *GADD45A*; oxidative stress related genes *NOX1, SOD1* and proapoptotic genes *HRK, NOXA, PUMA, DR5*. Taken together, the results suggest that Pd complex causes oxidative stress leading to DNA damage-mediated cell cycle arrest and apoptotic cell death.

Conclusion: Our palladium complex is a promising therapeutic agent for a specific subtype (Ovsaho) of ovarian cancer, which deserves further attention for *in vivo* proof-of-concept studies.

Poster Presentation – 63

Hydrocephalus microenvironment; A Revolutionary Era in the Diagnosis of Brain Tumors

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Background: Cerebral hypoxia is neurologically considered as a ventricular dilatation with hypoxic-anoxic brain damage, which is a direct consequence of high intracranial pressure, subsequently causing a disturbed blood-brain barrier/Cerebrospinal Fluid-blood barrier (CSF). Cerebral hypoxia occurs in approximately 0.1-0.6% of live births, with a swift increase in the incidence rate worldwide. Current therapeutic approaches include surgery, pharmacotherapies, and CSF shunts, not being beneficial for all of patients with cerebral hypoxia due to their low efficacy and some severe side effects. These challenges lead basic researchers and clinical specialists toward a deeper understanding on the cellular and molecular mechanisms and the inflammatory milieu involved in the immunopathogenesis of cerebral hypoxia. Immunopathophysiologically, this acute hypoxia-ischemia provokes an intravascular inflammatory cascade, which is amplified by the infiltration and functionalities of the resident immune cells, an induced expression of inflammatory cytokines/chemokines (IL-1α, 4, 6, 12, TNF-α), as well as hyperacidity-tumor-associated enzymes (Carbonic Anhydrases (CA) VII, IX, and XII) in the brain parenchyma mediated by Reactive Oxygen Species (ROS) compared to healthy infants, leading to the secondary brain tissue injuries such as hydrocephalus due to ependymal gliosis, arachnoiditis, and fibrotic blockage of CSF pathways. Those CA and several ion transporters are involved in CSF secretion, accentuating abilities of CA inhibitors to reduce CSF secretion through the choroid plexus, parallelable to a reduced CSF production.

Methods: In this review study, the authors examined a wide range of literature to demonstrate the strong correlations between hydrocephalus, brain tumors, hyperacidity/inflammatory markers, and their therapeutic options in a paraclinical settings.

Results: Hydrocephalus is associated with the activation of pro-inflammatory cytokines (CA-VII, CA-IX, CA-XII, IL-18, and IFN-γ) and hyperacidity biomarkers in CSF, while CSF biomarkers for apoptosis (sFasL) remained unchanged. The results of a large number of recent studies suggest that inhibition of receptor kinases in the brain tumor-associated microenvironment (anti-inflammatory immunotherapeutics) in combination with CSF shunting simultaneously contributes to the protection of brain tissue from cerebral hypoxia.

Conclusion: Molecular signaling may offer promising opportunities to manipulate the immunological microenvironment of hydrocephalus to transform it from a lifelong neurological disease into a

preventable neuroinflammatory disease. An interdisciplinary collaboration and further investigations between translational/alternative/molecular medicine specialists, immunologists, cancer biologists, molecular biologists, pediatricians, neurosurgeons, and oncologists are highly recommended.

Key words: Acidosis, Carbonic Anhydrase, Cerebrospinal Fluid Secretion, Hydrocephalus.

Fluorescent Warriors: Design and Evaluation of Novel Isatin-Based Compounds as Dual-Action Agents Against Breast Cancer

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Introduction and Aim: Cancer remains a major global health concern, with breast cancer being the most commonly diagnosed malignancy in women and a leading cause of cancer- related mortality. In response to the urgent demand for new therapeutic agents, this study reports the design, synthesis, and biological evaluation of seven novel isatin-derived
fluorescent compounds as potential anticancer agents.

Materials and Methods: The compounds were synthesized via a multi-step process with 1,8-naphthalimide, to modulate their fluorescence and cytotoxic properties. All seven compounds were structurally characterized using UV-Vis, FT-IR, ^{1}H NMR, confirming their expected molecular frameworks. The in vitro cytotoxic activity of the compounds was assessed against the MCF-7 human breast cancer cell line using the MTT assay.

Results: At 24th hour, compounds C and H exhibited the most potent cytotoxicity against MCF-7 cells, with low IC_{50} values of 1.77 μM and 3.85 μM, respectively, indicating strong early antiproliferative effects. By 48 th hour other compounds also showed marked improvement in potency, with IC_{50} values dropping to below 21 μM. Confocal laser scanning microscopy revealed efficient cellular uptake of this substance, with strong cytoplasmic fluorescence, indicating its potential for bioimaging applications alongside therapeutic use.

Conclusion: These results suggest that isatin-based fluorescent compounds, particularly C and H, hold significant promise as dual-function anticancer agents capable of both therapeutic action and cellular imaging. Further mechanistic and in vivo studies are recommended to advance these compounds toward clinical relevance.

Poster Presentation – 66

2B ve 3B *in vitro* kültür ortamında farklı stratejiler ile geliştirilen Gemcitabin direnç mekanizmasının kolanjiyokarsinoma hücre hatları özelinde araştırılması

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Kolanjiyokarsinom (KKA), karaciğer kanserleri arasında en sık görülen 2. kanser türü olarak bilinmekte ve tanıdan sonra 5-yıllık sağkalım oranı %25 seviyesindedir. Diğer kanser türlerine kıyasla daha nadir görülmektedir. Birinci basamak KKA tedavisinde Gemcitabin uygulanır ve Gemcitabin'e bağlı gelişen ilaç direnci sağkalım oranını etkileyen en önemli parametrelerden biridir. Bu noktada Gemcitabin'e bağlı direnç mekanizmasını moleküler seviyede anlamak ve aydınlatabilmek için farklı moleküler arka profillere sahip HuCC-T1 ve CC-LP-1 hücre hatlarında hem 2B hem de 3B *in vitro* kültür ortamında Gemcitabin'e maruz bırakılarak direnç gelişim süreçleri incelendi. Uyguladığımız farklı doz-süre kombinasyonları ile uygulama stratejileri arasındaki etkinlik farkları ise Sülforodamin B (2B in vitro) ve adenozin trifosfat (3B in vitro) aracılı canlılık testleri ile değerlendirildi. Gemcitabin'in hücre içerisinde metabolize olma süresi göz önüne alındığında 0-25-50-100 μM ve 0-1000 μM doz aralıklarında en etkili sonucun 72 saat uygulama süresinde alındığını gösterildi. Uzun süreli Gemcitabin mağruziyeti için başlangıç dozları 25 ve 50 μM seçilerek, aç/kapa yaklaşımı ile direnç gelişim süreçleri başlatılan intrahepatik HuCC-T1 ve ekstrahepatik CC-LP-1 hücre hatlarında direnç gelişim süreci başlatıldı ve belirli zaman aralıklarında Gemcitabin dozu 2-kat arttırılarak süreç halen devam etmektedir. Bu durumdan farklı olarak, Gemcitabin başlangıç dozu 100 μM seçildiğinde hücrelerin anatomik sınıflandırılması ve moleküler profillemeden bağımsız her iki hücre hattında direnç gelişim sürecinin devam ettirilemedi gözlemlendi. Kolanjiyokarsinoma hücre hatlarında Gemctiabin direnc sürecinin moleküler seyivede stabilize edilmesinin ardından gerçekleştirilecek olan bu süreçte rol oynayan moleküler mekanizmalarının aydınlatılması ve detaylandırılması için transkriptom analizleri gerçekleştirilecektir.

Anahtar kelimeler: Kolanjiyokarsinoma; Gemcitabin; Kemoterapötik Direnci; HuCC-T1; CC-LP-1

Salinomycin Overcomes Taxol-Resistance in Head and Neck Cancer Cells by Inhibiting Viability, Clonogenic Potential and Migration

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Introduction and Aim: Head and neck squamous cell carcinoma (HNSCC) is an aggressive malignancy with limited treatment options due to the emergence of drug resistance. Paclitaxel (Taxol) is a commonly used agent in the management of HNSCC; however, its effectiveness is frequently compromised by the development of resistance. Salinomycin, an ionophore known for its antibacterial and anticancer properties, has shown promising results in reducing cancer stem cells, particularly in breast cancer [1, 2]. Nevertheless, its potential efficacy in paclitaxel-resistant HNSCC cells remains uncertain. The present study aims to investigate the effects of salinomycin on cell viability, migration, and colony formation in paclitaxel-resistant HNSCC cells.

Material and Methods: To evaluate the effects of salinomycin on FaDu and SCC-9 taxol-resistant cells, several assays were conducted, including cell viability, scratch, and colony formation assays. The cells were treated with salinomycin for 24 and 48 hours, and cell viability was assessed using the CVDK-8 assay. The scratch assay measured cell migration following treatment with salinomycin and paclitaxel at their respective IC_{50} doses. Finally, colony formation was analyzed to determine the impact on various colony types.

Results: Salinomycin was found to significantly affect the viability of both FaDu and SCC-9 taxol-resistant cells, exhibiting a dose- and time-dependent response. The scratch assay demonstrated that salinomycin inhibited cell migration, while the colony formation assay revealed a decrease in holoclones and meroclones in taxol-resistant cells, accompanied by an increase in paraclones.

Discussion: The present study demonstrated that salinomycin inhibits proliferation, migration, and colony formation in HNSCC cells. The reduction of holoclones, which possess cancer stem cell properties, suggests that salinomycin may directly target cancer stem cells. Concurrent findings in other cancers underscore the potential of salinomycin as an effective anticancer agent. Further research is necessary to explore its mechanisms and therapeutic potential in resistant HNSCC cases.

[1] Q. Liu, J. Sun, Q. Luo, Y. Ju, G. Song, Salinomycin Suppresses Tumorigenicity of Liver Cancer Stem Cells and Wnt/Beta-catenin Signaling, Curr Stem Cell Res Ther, 16 (2021) 630-637.

[2] T.T. Mai, A. Hamaï, A. Hienzsch, T. Cañeque, S. Müller, J. Wicinski, O. Cabaud, C. Leroy, A. David, V. Acevedo, A. Ryo, C. Ginestier, D. Birnbaum, E. Charafe-Jauffret, P. Codogno, M. Mehrpour, R. Rodriguez, Salinomycin kills cancer stem cells by sequestering iron in lysosomes, Nat Chem, 9 (2017) 1025-1033.

Poster Presentation – 68

Combined effects of ranolazine and a tyrosine kinase inhibitor (AG1478) on human breast cancer cell invasiveness

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Introduction and Aim: Triple-negative breast cancer (TNBC) is the most aggressive and therapeutically challenging subtype of breast cancer (BCa), with most patients dying due to untreatable metastasis. Consequently, there is an urgent need to develop new anti-metastatic strategies. This project is based on evidence showing (i) that epidermal growth factor (EGF) regulates expression and activity of voltage-gated sodium channels (VGSCs) and (ii) that VGSC activity promotes (may even initiate) metastasis in BCa. We therefore questioned whether targeting simultaneously both pathways would be synergistic in inhibiting invasiveness of MDA-MB-231 cells used as an in vitro model of TNBC.

Materials and Methods: The response of MDA-MB-231 cells to different doses of the VGSC inhibitor ranolazine (1.25, 2.5 and 5 μM) and the EGF receptor inhibitor AG1478 (5 and 10 μM) was evaluated under hypoxic conditions (1% O_2). As functional assays, proliferation and Matrigel invasiveness were measured using MTT and Boyden chambers, respectively.

Results: Ranolazine and AG1478 individually exhibited an anti-invasive effect significantly in a dose-dependent manner without affecting proliferative activity. A synergistic effect was observed at low doses. Thus, although 1.25 μM ranolazine alone did not affect invasion, combination with 5 μM AG1478 suppressed invasiveness significantly by 58% ($p < 0.0001$). This effect of the combination on invasion was significantly greater than that of equimolar AG1478 alone (29%; $p < 0.05$).

Discussion: Our data demonstrate that BCa invasiveness can be effectively suppressed by clinically relevant doses ($\leq$5μM) of ranolazine, supporting the potential repurposing of this drug as an anti-metastatic agent[1]. Furthermore, the effective dose of ranolazine can be lowered significantly by synergistic combination with a tyrosine kinase inhibitor. This synergy not only reduces the possible side effects of ranolazine but also suggests a potential interplay between these pathways. Additional work is required to elucidate the molecular mechanism(s).

Key words: Anti-metastatic, drug combinations, drug repurposing, voltage-gated sodium channels

Reference

1. Djamgoz MBA (2024). Ranolazine: a potential anti-metastatic drug targeting voltage-gated sodium channels. Br J Cancer; 130(9):1415-1419.

Poster Presentation – 69

Synergistic Antiproliferative Effect of FX-11 and Benztropine Combination via EMT Modulation in Pancreatic Cancer Cells

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Introduction: Pancreatic cancer is an aggressive malignancy with poor prognosis and limited treatment options. Lactate dehydrogenase A (LDHA) plays a key role in cancer metabolism and is often overexpressed in tumors, contributing to their progression and resistance to treatment. Benztropine, a drug used for Parkinson's disease, has recently shown anticancer potential by targeting cancer cell plasticity. This study investigates whether combining LDHA inhibition with benztropine can produce a synergistic effect in pancreatic cancer, particularly through epithelial-to-mesenchymal transition (EMT) pathways.

Methods: A drug library of 1,450 FDA-approved anticancer compounds was screened in combination with the LDHA inhibitor FX-11 in the PANC-1 pancreatic adenocarcinoma cell line. Benztropine, identified as a promising compound, was further tested in combination with FX-11 across PANC-1, MIA PaCa-2, and AsPC-1 cells. Synergy was evaluated using CellTiter-Glo assays and colony formation assays (CFA). EMT was induced with TGF-β, and the expression of EMT markers was analyzed by qPCR and western blotting. Invasion and spheroid formation assays were also conducted.

Results: Combining FX-11 and benztropine resulted in a significant synergistic effect in all three cell lines, reducing cell proliferation, colony formation, and spheroid size ($p < 0.05$). After EMT induction, the combination treatment reduced the expression of EMT-related transcription factors Snail and Slug ($p < 0.05$). Furthermore, the combination therapy significantly reduced the invasive potential of the cells ($p < 0.05$).

Discussion: The results demonstrate that combining LDHA inhibition with benztropine inhibits tumor growth and invasiveness, likely through downregulation of key EMT regulators. This combination may represent a novel therapeutic strategy for targeting pancreatic cancer progression and metastasis.

Poster Presentation – 70

Dubermatinib may enhance the anti-cancer efficacy of gemcitabine on Panc-1 cells

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Introduction and Aim: Pancreatic adenocarcinoma is one of the most challenging malignancies to treat due to its high invasive potential and early metastasis ability. AXL, a member of the receptor tyrosine kinases, is a potential therapeutic target for pancreatic adenocarcinoma due to its critical roles in tumor progression, metastasis, and treatment resistance. This study investigated the efficacy of dubermatinib, an AXL inhibitor, combined with gemcitabine in human pancreatic cancer cell lines Panc-1.

Materials and Methods: Panc-1 cells were treated with gemcitabine (GEM), dubermatinib (TP), GEM+TP combination, and a non-treated Ctrl group. Cell viability was determined by SRB test 72 hours after drug administration. Effective drug combinations were determined by Synergyfinder analysis. To evaluate the effect of the drug combination showing synergistic effects on apoptosis, Bcl-2 and Caspase-3 expression levels were determined by qRT-PCR. A wound healing test and colony formation analysis were performed to determine the anti-cancer effects of the synergistic combined treatment. Student's *t*-test performed statistical analysis, and $p<0.05$ was considered significant.

Results: In the Panc-1 cell line, the combination of 0.5 μM GEM and 20 nM TP was found to have a synergistic effect. This combination treatment did not change Caspase-3 and Bcl-2 in the apoptotic process, but it was determined that it reduced the colony formation ability and wound healing process compared to monotherapy.

Discussion: The findings suggest that Panc-1 cells may resist cell death by apoptotic pathways under certain conditions and support the investigation of dubermatinib's drug potential in pancreatic cancer.

Key words: Panc-1, gemcitabine, dubermatinib, drug combination

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Poster Presentation – 71

An Already Prescribed Antidepressant, Vortioxetine, Can Be Considered as a Trustworthy Partner of a Novel Combinatorial Therapy for Ovarian Cancer Patients

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Introduction and Aim: Ovarian cancer (OV) has a high mortality due to its late-stage diagnosis. It is reported that the annual average number of new cases and death rate is 324,603 and 206,956, respectively (Ferlay J, 2022). Vortioxetine, a multi-modal antidepressant, is considered a traditional selective serotonin inhibitor (SSI) that effectively directs different serotonin receptors such as 5-HT_1 agonist and 5-HT_3 antagonist (Sanchez C & 25016186., 2014). Besides, it is known that vortioxetine is one of the highly prescribed drugs for OV patients. This research aims to investigate the impact of vortioxetine *in silico* to determine whether it may cause a synergistic effect with the commonly preferred drugs in OV, olaparib, carboplatin, and niraparib.

Materials and Methods: Literature was searched to determine the target proteins (TPs), which were then docked first to vortioxetine and next to olaparib/carboplatin/niraparib. The molecular docking (MD) analysis was repeated by changing the ligand order. Autodock4 and Autodock Vina were used to compare the results. The impact of the multi-docking was evaluated by their binding energy (ΔG) values.

Results: TPs were first docked to vortioxetine, and the achieved complex was further docked to olaparib/carboplatin/niraparib or vice versa. Considering the binding energy (ΔG) values obtained, we observed that multi-docking enhanced either the binding of olaparib/niraparib if the TPs are previously vortioxetine-docked or the binding of vortioxetine if the TPS are previously carboplatin-docked. For the TP (PDBI: 8HOG), it was observed that the multi-docking enhanced the binding scores regardless of the ligand order.

Discussion: The MD results suggest that vortioxetine may have different interactions with FDA-approved OV drugs depending on the binding order. Vortioxetine-involved therapy protocols against OV could be an alternative to enhance the anti-cancer effect of olaparib, carboplatin, niraparib. Furthermore, there is a potential to reach out to a combinatorial therapy relying on this synergy.

Key words: Ovarian cancer, Vortioxetine, Olaparib, Niraparib, Molecular Docking, Synergic effect

Poster Presentation – 72

Kemoterapi Dirençli Akciğer Kanseri Hücrelerinde Fingolimodun Sitotoksik Ve Proapoptotik Etkileri

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Giriş ve Amaç: Akciğer kanserinin en yaygın kanser türleri arasında ilk sırada yer aldığı ve küçük hücreli dışı akciğer kanserinin (KHDAK) tüm akciğer kanser vakalarının yaklaşık %85'ini oluşturduğu bilinmektedir. Hastaların %15'inde 5 yıl ve üzeri sağ kalım görülmektedir. Standart kemoterapi ajanlarından cisplatin akciğer ve bir çok farklı kanserin tedavisinde kullanılmaktadır. Cisplatinin birçok farklı mekanizma ile antikanser etki göstermesine rağmen tedavi sürecinde gelişen direnç tedavi başarısını olumsuz etkilemekte ve alternatif etkin tedavi seçeneklerine ihtiyaç duyulmaktadır. Fingolimod, sfingozin-1 fosfat reseptörünün fonksiyonel antagonizması yoluyla T hücrelerini lenf düğümlerine hapseden multipl skleroz için klinik olarak onaylanmış bir immünomodülatördür ve tedavi seçeneği olarak potansiyeli vurgulanmaktadır. Bu çalışmada cisplatin direci oluşturulmuş insan KHDAK hücreleri A549'da fingolimodun sitotoksik ve proapoptotik etkileri direç kazandırılmamış A549 hücreleri ile karşılaştırmalı olarak araştırılmıştır.

Materyal ve Metodlar: Sitotoksik etki MTT tekniği ile poapoptotik etkiler ise anneksin V ve kaspaz 3/7 testleri ile flow sitometride araştırılmıştır.

Bulgular: A549 hücrelerinde cisplatinin IC_{50} değerleri 24, 48 ve 72 saat için sırasıyla 24.7µM, 5.12µM ve 2.28µM, Fingolimod için 6.17µM, 5.21µM ve 2.32µM olarak bulunmuştur. Cisplatin dirençli A549 hücrelerinde cisplatinin IC_{50} değerleri 24, 48 ve 72 saat için sırasıyla 19.27µM, 18.36µM ve 19.9µM, fingolimod için ise 26.04 µM, 22.15 µM ve 26.39 µM olarak saptanmıştır. Fingolimod ve cisplatinin proapoptotik etkisi tespit edilmiştir.

Sonuç: Dirençsiz A549 hücrelerinde cisplatin ve fingolimod doza ve zamana bağlı sitotoksisite göstermiştir. Cisplatin dirençli A549 hücrelerinde ise sitotoksik etki doza bağlı olarak tespit edilmiştir. Cisplatin dirençli hücrelerde fingolimod proapoptotik etki göstermiştir. Sonuç olarak fingolimodun daha ileri araştırmalardan sonra kemoterapi dirençli akciğer kanser hücrelerinde etkin tedavi seçeneği sunabileceği bulguları ortaya konulmuştur.

Anahtar kelimeler: A549; Cisplatin; Fingolimod; Direnç

Poster Presentation – 73

İnsan Somatik Hibrit Hücrelerinde Bevacizumab Ve Carmofurun Hücre Canliliğina Etkileri

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Giriş ve Amaç: İnsan somatik hibrit hücre hattı EAhy926 endotelyal hücrelerinden geliştirilmiştir. Polietilen glikol stresi kullanılarak insan endotel hücreleri insan küçük hücreli dışı akciğer kanseri hücreleri A549 ile füzyonu sonucunda oluşturulan hücre hattıdır. Bu hücreler anjiyogenez, hemostaz ve inflamasyon gibi süreçlerde bazı farklılaşmış işlevleri yerine getirmektedir. Bevacizumabın doğrudan kanser hücrelerine bir etkisi bulunmamaktadır. Tümörü besleyen kan damarlarının gelişimini engelleyerek tümörün büyümesi yavaşlatılır. Bevacizumab kemoterapi sürecinde stansart kemoterapi ilaçları ile birlikte yan tedavi ajanı olarak kullanılmaktadır. Carmofur, DNA sentezini bozarak hücre bölünmesini engeller, apoptozu indükler, hücrelerin sentez fazında kalmasını sağlayarak hücre siklusunu engeller. Bunun sonucunda kanser hücrelerinde antiproliferatif etki meydana gelir. Bu çalışmada bevacizumab ve carmofurun EAhy926 hücrelerinde hücre canlılığı üzerine etkileri araştırılmıştır.

Materyal ve Metodlar: Hücre canlılığına etkilerin araştırılmasında MTT ve anneksin V teknikleri kullanılmıştır.

Bulgular: EA.hy926 hücrelerinde bevacizumabın 24, 48 ve 72 saatte sitotoksik etkisi test edilen dozlarda bulunamamıştır. Carmofurun IC_{50} değerleri 24, 48 ve 72 saat için sırasıyla 12.04 µM, 9.92 µM ve 8.37 µM olarak bulunmuştur. Anneksin V test bulguları carmofur ve bevacizumabın apoptozu indüklediğini göstermiştir.

Sonuç: EA.hy926 hücrelerinde carmofurun konsantrasyon ve zamana bağlı olarak sitotoksik ve proapoptotik etkileri saptanmıştır. Sonuç olarak, carmofur ve bevacizumabın insan somatik hibrit hücreleri üzerinde hücre ölüm mekanizmalarının araştırılması için daha ileri farmasötik ve farmakokinetik etkiler üzerine çalışmalarda kullanılması için önerilmektedir.

Poster Presentation – 74

Modulation of Angiogenic Activity with 24-Epibrassinolide and/or Temozolomide Treatment in HUVEC Cells

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Glioblastoma (GBM) is the most aggressive type of brain tumor among gliomas. The survival rate of GBM patients is typically less than two years. The current treatment of GBM, involves temozolomide (TMZ) during chemotherapy. TMZ exerts its cytotoxic effect through DNA methylation, leading to DNA fragmentation and cell death. However, the complex structure of the tumor microenvironment contributes to the development of TMZ resistance, making GBM treatment more challenging. The hypoxic microenvironment of malignant gliomas promotes tumor angiogenesis, contributing to tumor progression. Angiogenesis, the formation of new blood vessels from pre-existing vasculature, occurs through endothelial cell proliferation and migration following the degradation of the basement membrane. Suppressing tumor angiogenesis offers new therapeutic approaches for GBM treatment. 24-Epibrassinolide (EBR), a steroid-derived agent belonging to the brassinosteroids family, exhibited anticancer properties in GBM cells via endoplasmic reticulum (ER) stress-induced apoptosis.

In this study, we evaluated the potential angiogenic effects of EBR and/or TMZ in HUVEC cells, representing an endothelial model of the tumor microenvironment. HUVEC cells treated with EBR and/or TMZ for 24 hours, was analyzed for the cell viability, cell survival, 2D and 3D colony formation assays. To evaluate angiogenic potential, tube formation and wound healing assays were performed. Additionally, the expression levels of angiogenesis-related genes and apoptotic markers were analyzed by western blotting. EBR and/or TMZ treatment significantly suppressed HUVEC cell migration and tube formation capacity. Moreover, a reduction in the expression levels of angiogenesis-related genes such as VEGF, VEGFA, VEGFR2, and p-VEGFR2 was observed. These findings suggest that EBR, in combination with TMZ, may inhibit angiogenesis and suppress VEGF-mediated angiogenic signaling. This positions EBR as a potential therapeutic agent for GBM treatment. Our study highlights the anti-angiogenic potential of EBR and sheds light on new treatment strategies for GBM management.

Key words: Glioblastoma, Tumor Microenvironment, 24-Epibrassinolide, Temozolomide, Endoplasmic Reticulum Stress, Angiogenesis

Poster Presentation – 75

Investigation of The Effects of TAS-115 on a 3D Triple Negative Breast Cancer Model

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Introduction and Aim: Triple-negative breast cancer (TNBC) is the most aggressive breast cancer subtype, lacking targeted therapies due to the absence of estrogen, progesterone, and human epidermal growth factor 2 expression. TAS-115, a multi-receptor tyrosine kinase inhibitor, blocks auto-fosforylation of c-MET/HGF and VEGFR, inhibiting associated signaling pathways such as PI3K/Akt/mTOR, thereby reducing cancer cell survival. No studies to date have evaluated TAS-115's efficacy in TNBC. In this study, we aimed to investigate the effects of TAS-115, both individually and in combination with doxorubicin (DOXO), on the c-MET/HGF and PI3K/Akt/mTOR pathways in a 3D heterotypic spheroid model was consisting of GFP^+ MDA-MB-231 cells and normal human lung fibroblasts (NHLF) The impact of TAS-115 on spheroids was assessed evaluating cell survival, proliferation, and cytokine responses.

Materials and Methods: TAS-115's influence on c-MET/HGF signaling and the PI3K/Akt/mTOR pathway, with emphasis on p-mTOR, was determined. The effects of TAS-115 on spheroid invasion and metastasis potential following 3D bioprinting were also investigated. Our study provides critical insights into the effects of TAS-115 on TNBC and NHLFs in a 3D microenvironment, evaluating tumor growth, spread, and cytokine responses.

Results: In the formed heterotypic spheroid model, following the treatment with TAS-115 both individually and in combination with DOXO, a decrease in cancer cell survival and proliferation was observed. Additionally, the expression of c-MET, p-c-MET, and p-mTOR, as well as pro-inflammatory cytokine responses, were significantly reduced. After 3D bioprinting, a marked reduction in the invasion and metastasis potential of the spheroids was also observed ($p<0.05$).

Discussion: This study provides critical insights into the effects of TAS-115 on TNBC and lung fibroblasts in a 3D microenvironment. These findings may pave the way for future preclinical and clinical investigations, potentially positioning TAS-115 as a novel therapeutic strategy for TNBC, either as a monotherapy or in combination with existing chemotherapeutic agents.

Key words: TNBC, Spheroid, 3D bioprinting, c-MET, TAS-115

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