CONGRESS

ABSTRACT BOOK

Welcome Message

Dear Colleagues,

On behalf of the Organizing Committee I am delighted to invite you to the 10th International Congress of Molecular Medicine that will be held in Çeşme-Izmir, Turkiye on 23rd - 27th of September 2024 under the auspices of the Turkish Society of Molecular Medicine.

Congress program will consist of outstanding lectures, including keynote talks, plenary sessions, oral & poster presentations & exhibition & workshops.

The congress biennial of molecular medicine is an important forum for researchers and clinicians from Turkiye and all around the world to focus on the latest developments in molecular medicine.

On the other hand, this year, in which we celebrate the 25th anniversary of the Turkish Society of Molecular Medicine, is of particular importance for our congress.

We will be looking forward to meet you in September 2024 for this congress we are organizing for the 10th time this year, with leading scientists in their field and researchers who will make their valuable contributions.

Prof. Dr. Umit Zeybek

Chair of the Turkish Society of Molecular Medicine

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X. International Congress of Molecular Medicine

23-27 September 2024
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INVITED SPEEKER PROGRAM

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24 September 2024 - Tuesday	
10:30 – 11:30	**PROTOCOL** - **Ümit Zeybek** - Congress President, Head of Turkish Molecular Medicine Association - **Kenan Türkdoğan** - Rector, Alanya Alaaddin Keykubat University - **Yusuf Baran** - Rector, İzmir Institute of Technology, Congress Honorary President **WELCOME NOTE** - **Yusuf Baran** Molecular Mechanisms of Drug Resistance
11:30 - 12:15	**PLENARY LECTURE** **Moderators: Bülent Özpolat** - **Mustafa Djamgöz** Cancer Neuroscience - A New Discipline in Oncology
13:00 – 15:00	**Panel 1: RNA Biology in Health and Diseases** **Moderators: Alper Tunga Özdemir** - **Alper Tunga Özdemir** Chimeric Antigen Receptor (CAR) Approaches in Autoimmune Diseases - **Bilge Özdemir** Mesenchymal Stem Cell Experiences in the Clinic - **Mustafa Diken** mRNA-based Cancer Vaccines - **Elif Diken** Single-Cell Insights into Immunotherapy Efficacy and Mechanisms
15:15 – 16:00	**KEYNOTE LECTURE** **Moderators: Akif Turna** - **Suresh C. Jhanwar** Cancer Genomics in Translational Research and Precision Medicine: A Brief Overview of Current Status and Future Prospects
16:15 – 18:15	**Panel 2: Health Informatics (Bioinformatics) & Artificial Intelligence in Health** **Moderators: Mükerrem Betül Yerer Aycan, Tunç Akkoç** - **Akif Turna** AI in Thoracic Surgery - **Mehmet Baysan** Systematic Analysis of Genetic Variant Identification and Pathogenicity Prediction - **Uzay Görmüş DeGrido** The Fundamentals and Sustainability of Future Science in the Medical and Research Laboratories - **Ceyda Açılan Ayhan** Epidrug Screening Identifies Type I PRMT Inhibitors as Modulators of Lysosomal Exocytosis and Drug Sensitivity in Cancers

25 September 2024 - Wednesday	
09:30 – 10:15	**KEYNOTE LECTURE** **Moderators: Gül Güner Akdoğan** - **Luciano Saso** Pharmacological Modulation of NRF2
10.30 – 12:30	**Panel 3: Advances in Natural Product Biochemistry: in Terms of Basic and Clinical Perspective and Nanomedicine** **Moderators: İlhan Yaylım, Ammad Ahmad Farooqi** - **Ammad Ahmad Farooqi** Targeting of Oncogenic Pathways by Natural Products: Underlying Mechanisms and Proof-of-Concept Animal Model Studies - **Suna Timur** In-Vitro Diagnostics and Nanomedicine - **Mükerrem Betül Yerer Aycan** Nano solutions for Big Problems: Targeted Drug Delivery Systems - **Burcu Okutucu** Biopolmer Based Nanoparticles for Metabolic Diseases
13:00 – 15:30	**Panel 4: Molecular Cancer Medicine; Past & Present, and Future Prospects and Medical Solutions** **Moderators: Hilal Koçdor, Zekiye S. Altun** - **Figen Zihnioğlu** Multifunctional Bioactive Peptides for Cancer Diagnosis and Therapy - **Safiye Aktaş** Fusion Analyzes and Clinical Significance in Next-Generation Sequencing in Tumor Tissue - **Güliz Armağan** A Novel Approach to Drug Resistance in Cancer: Ferroptosis - **Yasemin Soysal** Wound Age Determination in the Perspective of Forensic Biology - **Özkan Doğanay** New Insight into Lung Function Using Novel Contrast MR: from Anatomical to Molecular Imaging
15:45 – 17:45	**Panel 5: Cell Signalling and Metabolism: New Trends in Basic and Clinical Approaches** **Moderators: Nuray Ulusu, Özlem Timirci Kahraman** - **Aylin Sepici Dinçel** Osteporosis Treatment via Wnt Signalling Pathway - **Mutay Aslan** Plasma Sphingolipidomic Profile in Insulin Resistance and Diabetic Dyslipidemia - **Tunç Akkoç** Cancer İmmunotherapy and CarT Cell - **Nihal Karakaş** Stem Cell Treatment Approaches for Covid19 and Possible Viral Pandemics

26 September 2024 - Thursday	
10:00 – 10:45	**KEYNOTE LECTURE** **Moderators: Engin Ulukaya** - **Bülent Özpolat** Development of Novel Targeted Therapies for Solid Cancers
11:00 – 12:30	**Panel 6: Nutrition and Molecular Medicine** **Moderators**: **Ali Osman Gürol, Gülsen Meral** - **Eugenia Bezirtzoglou** Functional Dairy Foods and Microbiota Modulation - **İrina Danilova** Beta-cells in Diabetes: New Look at the Old Problem - **Christina Tsigalou** Mediterranean Dietary Patterns and Immunonutrition as Potential Intervention upon Gut Microbiome in IBD. Wishful Thinking or a Vision of the Future?
13:00 – 15:30	**Panel 7: Molecular Aspects in Forensic Sciences** **Moderators: Emel Hülya Yükseloğlu, Mutay Aslan** - **Itır Tarı Cömert** Genetic Signatures: Revealing Insights into Criminal Profiling and Violence - **Ceren Özbaşaran Tan** The Psychological Impact of Genetic Testing - **Meryem Ebedi** Exploring Addiction, Violence, and Genetic Insights in Forensic Science - **Nazlı Hölümen** Celebrating Uniqueness: The Power of Forensic Genetics in Individual Identification - **Ömer Karataş** Unveiling the Genetic Code: Exploring Forensic Science at the DNA Level
15:45 – 17:15	**Panel 8: Anti-Cancer Therapies; Cilinical and Molecular Approaches** **Moderators: Banu İşbilen Başok, Aylin Sepici Dinçel** - **Engin Ulukaya** Critical Considerations for Preclinical Evaluation of Newly Synthesized Anticancer Compounds - **Metin Kurtoğlu** Advanced Therapeutic Medicinal Product: Advantages and Disadvantages - **Nuray Ulusu** Metabolic Plasticity & Dormant Status of Cancer Cells

27 September 2024 - Friday	
09:30 – 10:15	**KEYNOTE LECTURE** **Moderators: Semra Demokan** - **Ahmad R. Bassiouny** Role of Long- noncoding RNA in Cancer and Neurodegenerative Diseases
10:30 – 12:30	**Panel 9: Biomarkers: Recent Hallmarks** **Moderators: Banu İşbilen Başok, Canan Cacına** - **Bünyamin Akgül** Long Non-coding RNAs in Cell Death and Survial - **Duygu Aydemir** Impact of the Metabolic Targets on the Cancer Treathment Regarging with Novel Cancer Death Pathways - **Yunus Akkoç** The Role of Autophagy in Tumor Microenvironment
12:30 - 14:00	**Closing and Award Ceremony**

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ORAL PRESENTATION PROGRAM

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24.09.2024 / 13:30-14:45

Oral Presentation Session I

Session Chairs: Özlem Timirci Kahraman, Cem Horozoğlu

- **Effects of Nanoplastics on Locomotor and Acetylcholinesterase Activities of Developing Zebrafish Embryos**
  Zülal Mızrak, Semanur Işıkoğlu, Merih Beler, Gizem Eğilmezer, Ismail Ünal, Derya Cansız, Ebru Emekli Alturfan

- **Relationship between Radio Frequency Electromagnetic Field Exposure and Developmental Pathways to Obesity in Zebrafish Embryos**
  Derya Cansız

- **Investigation of Morphological and Behavioral Alterations in Hypoxia-induced Zebrafish Embryos**
  Efruz Irem Akkuş Yaylamış, Derya Cansız, Ismail Ünal, Merih Beler, Müjgan Cengiz, Ebru Emekli Alturfan

- **Investigation of the Effect of Nanoplastic Exposure on The Oxidant-Antioxidant Balance in Zebrafish Embryos**
  Merih Beler, Ismail Ünal, Derya Cansız, Gizem Eğilmezer, Ebru Emekli Alturfan

- **Differential Effects of Vitamin K1 and Vitamin K1 on Zebrafish Embryogenesis**
  Semanur Işıkoğlu, Zülal Mızrak, Merih Beler, Gizem Eğilmezer, Efruz İrem Akkuş, İsmail Ünal, Derya Cansız, Ebru Emekli Alturfan

24.09.2024 / 15:00-16:15

Oral Presentation Session II

Session Chairs: Beyza Özçınar, Semra Koçtürk

- **Hedgehog Pathway is a Regulator of Stemness in Her2-Positive Trastuzumab Resistant Breast Cancer**
  Idris Er, Asiye Busra Boz Er

- **Targeting ITGβ3 to Overcome Trastuzumab Resistance in HER2-Positive Breast Cancer: Insights into TGF-β Signaling and Migration**
  Asiye Busra Boz Er, Idris Er

- **Investigation of The Effects of Doxorubicin on MTR, BCAT1 And PHGDH Genes In Mcf-7 Cell Line**
  Arda Kebapcı, Levent Gülüm, Kezban Uçar Çifçi, Merve Nur Al, Yusuf Tutar

- **Pharmacogenomics and Its Influence on Therapy Response and Toxicity**
  Mahmoud Abudayyak, Gül Özhan

- **Investigation of Gene Fusions and Rearrangements In Thyroid Malignancies In The Turkish Population**
  Burcu Çelikel, Gulcin Yegen, Nihat Aksakal, Semen Onder, S. Umit Zeybek

24.09.2024 / 16:45-18:00

Oral Presentation Session III

Session Chairs: Cem Horozoğlu, Gülper Nacarkahya

- **Exploring lipidomic shifts in acute myeloid leukemia cells: The impact of dual inhibition of Mcl-1 and sphingolipid metabolism**
  Melis Kartal Yandim, Mesut Bilgin

- **Effects of PGR gene expression and H770H (rs1042839) mutation on tumor and clinical characteristics in glioma**
  Özlem Kurnaz Gömleksiz, Merve Nur Aksakal, Adil Meric Altınöz, Mahmut Özden, Melih Bozkurt

- **Evaluation of Nrf2 Gene and Keap 1 Enzyme Levels İn Bladder Cancer**
  Mehmet Aydın Dağdeviren, Mehmet Özaslan, Sibel Bayıl Oğuzkan, Ömer Eronat

- **Investigation of Co-expression of lncRNA SNHG1 and miR-153-3p in Tumor and Tumor Microenvironment of Gastric Cancer Cases**
  Şafak Şener, Cem Horozoglu, Hazal Karadag, Asli Yildiz, Mehmet Tolgahan Hakan, Soykan Arikan, Ilhan Yaylim

- **Possible Correlations between OX40 rs17568 A/G Gene Variant and sOX40 serum levels in Gastric Cancer patients**
  Hajir Moosa Mohammed Al Khafaji, Ali Elselmo, İslim Kaleler, Dilara Sönmez, Mehmet Tolgahan Hakan, Cem Horozoğlu, Özlem Küçükhüseyin, Soykan Arıkan, Filiz Akyüz, İlhan Yaylım

25.09.2024 / 13:00-14:15

Oral Presentation Session IV

Session Chairs: Canan Cacına, Özlem Kurnaz Gömleksiz

- **Exploring the role of epigenetic regulators in Paclitaxel-Resistant NSCLC**
  Arda Işıklar, Buse Cevatemre, Hamzah Syed, Ceyda Açılan Ayhan

- **Ylang ylang oil might induce mitophagy in lung cancer cell lines**
  Baris Ertugrul, Göksu Kasarcı Kavsara, Tugba Buse Şentürk, Timur Hakan Barak, Sinem Bireller, Bedia Cakmakoglu

- **Effects of PPAR-gamma Agonists on in-vitro Diabetic Models of Oestrogen-Positive Breast Cancer**
  Melike Sağ, Hülya Yılmaz Aydoğan, Oğuz Öztürk

- **A First Preliminary Report: Potential Implications of IDO1 Expression on Soluble Tryptophan and Tryptophan Catabolites in Gastric Tumors and Tumor Microenvironment**
  Cem Horozoglu, Mehmet Tolgahan Hakan, Safak Sener, Dilara Sonmez Zor, Fikret Aktas, Ozlem Kucukhuseyin, Soykan Arikan, Filiz Akyuz, Ilhan Yaylim

- **New and Effective Compounds for Alzheimer's Disease and Cancer Therapy: Design, Synthesis and Biological Evaluation Studies**
  Kadircan Ural, Ferah Comert Onder

25.09.2024 / 16:45-18:15

Oral Presentation Session V

Session Chairs: Sacide Pehlivan, Gülbu Isıtmangil

- **Investigation of LEP, LEPR Variants, and LEP Methylation In Knee Osteoarthritis**
  Yasemin Oyacı, Dicle Rotinda Özdaş Sevgin, Mustafa Pehlivan, Demirhan Dıraçoğlu, Fatima Ceren Tuncel, Sacide Pehlivan

- **Determining the association between GDF-15 gene variants and Type 2 Diabetes: A hospital-based case-control study**
  Emine Yagci, Gamze Zengin, Cansu Ozbayer, Melike Bayindir Ureten, Medine Nur Kebapci, Irfan Degirmenci, Hulyam Kurt

- **Evaluation of rs1244378045, rs767450259 and rs750556128 Mutations in Terms of Polymorphism in Diabetic Obese and Non-Diabetic Obese Individuals**
  Saadet Busra Aksoyer Sezgin, Sermin Durak, Faruk Celik, Varol Guler, Aysegul Sarıkaya, Umit Zeybek

- **Comparison of Symptoms with Mutation Results in Patients with FMF Preliminary Diagnosis in the Bolu Region**
  Ali Osman Arslan, Murat Dıramalı, Murat Alışık

- **Impact of *IFNAR1* Gene Variations on Epilepsy: Interaction of Carbamazepine and Levetiracetam in Treatment Outcomes**
  Kübra Çiğdem Pekkoç Uyanık, Zeynep Gizem Todurga Seven, Erhan Raşit Agay

- **SCUBE-1 as a biomarker predictor for the home follow up and hospitalization of SARS-CoV-2 patients**
  Mustafa Kerem Özyavuz, Selçuk Eren Çanakçı, Kenan Ahmet Türkdoğan, Faruk Çelik, Mehmet Mesut Sönmez, İbrahim Yılmaz, Ali Osman Arslan, Abdullah Emre Güner, Şakir Ümit Zeybek

26.09.2024 / 15:00-16:15

Oral Presentation Session VI

Session Chairs: Özlem Timirci Kahraman, Özlem Kurnaz Gömleksiz

- ***In Silico*, Synthesis, *In Vitro* Enzyme-Activity of New and Potential Inhibitor Candidates for Alzheimer's Treatment and Their Antiproliferative Effects**
  Merve Sıkık, Ferah Comert Onder

- **Testing of 1.7A2UCOE, 1.2A2UCOE and O.5UCOE Universal Chromatin Opening Elements (UCOE) Derived from Hnrpa2b1-Cbx3 Reference Gene Loci on Human Stem Cells (iPS Cells)**
  Omer Faruk Anakok, Livanur Yücel, Hassana Adamou Ali

- **Effects of the VDR rs757343 (T>A) polymorphism in MODY patients**
  Şura Edanur Sağlam, Beyzanur Şimşek Çetin, Aref Khalkhali, Bita Rostami, Ilhan Satman, Nurdan Gül, Özlem Kurnaz Gömleksiz, Hülya Yılmaz Akdoğan, Deniz Kanca Demirci

- **Impaired CB1 Receptor Function and Endocannabinoid Disruption Enhance Simvastatin-Induced Skeletal Muscle Toxicity**
  Hilal Kalkan, Elisabetta Panza, Ester Pagano, Giuseppe Ercolano, Claudia Moriello, Fabiana Piscitelli, Mónika Sztretye, Raffaele Capasso, Vincenzo Di Marzo, Fabio Arturo Iannotti

- **Photodynamic Therapeutic effects of Verteporfin on foveal retinal vessels in Age-related Macular Degeneration:: A year result of the retrospective study planned for three years**
  Ayhan Önal

26.09.2024 / 16:30-18:00

Oral Presentation Session VII

Session Chairs: Canan Cacına, Karolin Yanar

- **Determination of the relationship between cholinergic activity and autoimmunity in patients with Hashimoto thyroiditis**
  Gulten Ates, Ismail Cem Sormaz

- **Effects of oxidative stress caused by methotrexate and aging on reproductive hormones**
  Şükriye Çalışkan, Şehkar Oktay

- **Comparison of the impact of oleuropein on adult female *Drosophila melanogaster* fed on sucrose and sucrose+fructose media**
  Karolin Yanar, Sevcan Kutlu, Melike Demir, Pınar Atukeren

- **Development and Clinical Validation of an Oxford Nanopore-Based Multigene Panel for the Diagnosis of Carnitine Cycle Defects**
  Gökçe Akan, Mehmet Cihan Balcı, Gülten Tuncel, Meryem Karaca, Hasan Hüseyin Kazan, Ahmet Caglar Ozketen, Ozge Ozgen, Asuman Gedikbaşı, Gulden Fatma Gokcay, Fatmahan Atalar

- **Comparative Evaluation of Immune Marker Expressions in Human Adipose Tissue MSCs Expressing Chimeric Cytokine Receptors**
  Sude Coşkun, Alper Tunga Özdemir, Rabia Bilge Özgül Özdemir, Mehmet Tolgahan Hakan, Nihat Aksakal, Ali Osman Gürol, İlhan Yaylım, Şakir Ümit Zeybek

- **Investigation of Umami Taste TR1/TR3 Receptor Expression Levels in Rat Peripheral Tissues in the NMDAR Hypofunction Model**
  Duygu Vardağlı, Karolin Yanar, Zeliha Emel Zengin

- **Evaluation of time-dependent molecular changes of thrombocyte concentrates prepared by apheresis method**
  Basma Alhamrouni Almuntasir, Basak Adaklı Aksoy, Ayca Dogan

Invited Speaker Summaries

Molecular Mechanisms of Drug Resistance

Yusuf Baran

Rector İzmir Institute of Technology, Department of Molecular Biology and Genetics

Chemotherapy is the most widely used treatment strategy for cancer, which is the second reason for human deaths after heart-related diseases. However, cellular resistance mechanisms developed by cancer cells and tissues in the beginning or proceeding times to apply anticancer agents is a significant problem preventing successful therapy. Resistance cancer cells develop to structurally and functionally different cytotoxic agents is called multi-drug resistance.

Drug resistance mechanisms have different molecular genetics and biochemical reasons depending on the applied drug and the type of cancer. Secondary genetic alterations and disorders in cancer cells may also result in drug resistance. That is why it is vital to study and consider all signaling pathways in multidrug resistance of cancer.

Multidrug resistance occurs via many unrelated mechanisms, such as overexpression of energy-dependent efflux proteins, decrease in uptake of the agents, increase or alteration in drug targets, alterations in cell cycle checkpoints, inactivation of the agents, compartmentalization of the agents, inhibition of apoptosis, increases in DNA repair mechanisms, problems related with drug metabolism and aberrant metabolism of bioactive sphingolipids. Exact elucidation of resistance mechanisms and molecular and biochemical approaches to overcome multidrug resistance have been a significant goal in cancer research. In this talk, I will explain the mechanisms contributing to multidrug resistance in cancer chemotherapy and touch on the approaches for reversing the resistance.

Cancer Neuroscience: A New Discipline in Oncology

Mustafa B A Djamgoz

Imperial College London, Department of Life Sciences, London SW7 2AZ, UK

Increasing evidence suggest that cancer cells and neurones are functionally associated, and this association is of significant pathophysiological significance. This burgeoning field, now called broadly “cancer neuroscience” encompasses two distinct areas depending on the nature of the association.

Intrinsic

This is seen most clearly in carcinomas, the most common type of cancer. Thus, in their cancerous state, epithelia exhibit several neuronal characteristics. These include antineuronal nuclear antibody, Hu antigen proteins (neurogenetic markers), neurone-specific enolase, aromatic l-amino acid decarboxylase, neuronal cell adhesion molecules, neurone-restrictive silencer factor, voltage-activated ion channels and neurotransmitter receptors. In particular, a range of carcinomas with strong metastatic ability express de novo voltage-gated sodium channels (VGSCs) which enable them to become electrically excited and generate Hodgkin-Huxley type action potentials (APs) [1]. In turn, it is the excitation that drives the cells’ invasive behaviour leading to metastasis. We called this the “CELEX model” [1]. Blocking the VGSC expression / activity suppresses invasiveness in vitro and full-blown metastasis in vivo.

Extrinsic

These include direct innervation as well as endogenous neuronal agents impacting cancer cells through the circulation [2]. Major nerve inputs are derived from the vagus nerve and the peripheral nervous system. Re the latter, sympathetic (adrenergic) and parasympathetic (cholinergic) nerves promote the early (proliferative) and later (invasive) stages of prostate cancer. Correspondingly, in prostate cancer patients, life expectancy is shorter when there is high level of nerve input and (ii) loss of the nerve connection in traffic accidents was shown to result in reduced risk of prostate cancer [3]. Amongst circulating neurotransmitters, some released from the central nervous system, dopamine has been studied in some depth. In an elegant in vivo study, dopamine released from the ventral tegmental area was shown to inhibit tumour development in a mouse model [4].

Clinical potential

Bioelectricity is one distinct area that connects cancer and neuroscience. As such, it promises to enable several different lines of clinical application in diagnostics and therapeutics. Very simply, the CELEX model would predict that occurrence of APs in a given primary tumour would mean that the cancer will metastasise. This could form the basis of an ‘electro-

oncogram'. Therapy would be possible (i) directly by modulating the nerve input to the tumour and/or (ii) indirectly by applying appropriate neuroactive drugs [5]. One such drug is ranolazine for which evidence all the way to humans suggests it would serve as an inhibitor of metastatic disease, the main cause of death from cancer [6]. This approach promises to maintain cancer in a non-metastatic state with which patients can live chronically.

References

1. Djamgoz MBA (2024a). Cancer Metastasis Rev. 2024 Jul 8. doi: 10.1007/s10555-024-10195-6.

2. Hutchings C et al. (2020). Biochim Biophys Acta Rev Cancer; 1874(2):188411. doi: 10.1016/j.bbcan.2020.188411.

3. Barbonetti A et al. (2018) Asian J Androl. 20(6):555-560. doi: 10.4103/aja.aja_31_18.

4. Ben-Shaanan TL et al. (2018). Nat Commun;9(1):2723. doi: 10.1038/s41467-018-05283-5.

5. Phillips JA et al. (2021). Bioelectricity; 3(1):14-26. doi: 10.1089/bioe.2020.0051.

6. Djamgoz MBA (2024b). Br J Cancer; 130(9):1415-1419. doi: 10.1038/s41416-024-02622-w.

Chimeric Antigen Receptor (CAR) Approaches in Autoimmune Diseases

Alper Tunga Ozdemir

Universitätsmedizin Johannes Gutenberg-Universität

While Chimeric Antigen Receptor (CAR) technology has shown remarkable success in cancer treatment, its potential to address autoimmune diseases is gaining significant traction. Autoimmune diseases, unlike cancer, result from the immune system mistakenly attacking the body's own tissues. CAR-based therapies offer a promising approach to re-educate immune cells to specifically suppress these harmful responses.

This presentation delves into the latest advancements in CAR technology tailored for autoimmune conditions such as systemic lupus erythematosus, rheumatoid arthritis, and multiple sclerosis. Key areas of focus include:

- Designing CAR-T cells to target specific autoimmune pathways.
- Utilizing CAR regulatory T cells (CAR-Tregs) to promote immune tolerance.
- Addressing the challenges in ensuring safety and efficacy in clinical applications.

Emerging preclinical and clinical data indicate that CAR approaches may not only alleviate symptoms but also induce long-term remission in patients with refractory autoimmune disorders. Harnessing the power of CAR technology holds the promise of transformative therapies that could fundamentally change the management of autoimmune diseases.

Mesenchymal Stem Cell Experiences in the Clinic

Bilge Ozdemir

Visiting Scientist at Department of Rheumatology and Immunology, Universitätsmedizin Johanes Gutenberg University Mainz

Chronic spontaneous urticaria (CSU) is a debilitating condition affecting 0.5-5% of the population. While antihistamines are the mainstay of treatment, a significant proportion of patients remain resistant to conventional therapies. This study explores the potential of mesenchymal stem cells (MSCs) as a novel therapeutic approach for refractory CSU.

We enrolled 10 refractory CSU patients who received autologous adipose tissue-derived MSCs and compared their response to 10 control patients receiving standard treatment. Over a six-month follow-up, patients receiving MSCs demonstrated a significant reduction in urticaria activity scores and drug use scores, suggesting improved symptom control and a potential for long-term remission.

Additionally, we investigated the effects of MSCs on immune cell subsets and cytokines. While MSCs did not significantly alter immune cell populations in the treatment group, the control group showed significant decreases in Th2 subset, TGF-β1, PGE2, IDO, and anti-FcεRI levels. These findings suggest that MSCs might exert their therapeutic effect through a distinct immunomodulatory mechanism.

Our data highlights the potential of MSCs as a promising therapeutic strategy for refractory CSU. Future research exploring the precise mechanisms of action and optimizing the treatment protocols holds immense promise for enhancing the lives of patients suffering from this challenging condition.

Cancer Genomics in Translational Research and Precision Medicine: A brief overview of current status and future prospects

Suresh C. Jhanwar

Memorial Sloan Kettering Cancer Center, Department of Pathology & Laboratory Medicine, New York, N Y 10065, USA

Cancer is a genetic disease is by now well recognized. Genomic analysis of cancer cells, therefore, has greatly enhanced our ability to identify genetic alterations associated with various cancer types, including both lympho- hematopoietic as well as solid tumors. Chronic myeloid leukemia (CML), based on the specific diagnostic genetic abnormality has served as a prototype disease to clearly demonstrate the significance of the genomic analysis of cancer in identifying targeted therapy. Such a success has provided extra ordinary opportunities to investigate the role of genetic abnormalities and the pathways amenable to targeted therapy, not only in blood cancers but solid tumors such as Lung, brain, colon, Renal, Breast cancers as well as other epithelial and mesenchymal tumors.

The main focus of this presentation is to illustrate the role of genomic analysis in targeting lung cancer, based on abnormalities or the pathways deregulated in tumor cells from individual patients. Lung cancer is one of the most common epithelial cancers associated with chronic inflammation due to cigarette smoking and other environmental carcinogens, and includes four distinct histologic type; non-small cell lung cancer (NSCLC); small cell lung cancer (SCLC) and squamous cell lung cancer. According to current estimates, 1.3 million cases of lung cancer are expected to be diagnosed worldwide annually, resulting in one million deaths annually. Since the discovery that patient's tumors with specific mutations in the EGFR may be sensitive to targeted therapeutic approach and the subsequent realization that the such mutations in the gene are not as prevalent, several cancer centers including ours initiated intense efforts to find other mutations or genomic alterations, which may serve as targets of specific therapy**.** Su**c**h efforts have successfully resulted in a battery of genes such as KRAS, ALK, C-MET, HER-2/neu, ROS1, etc., which have helped oncologists to triage the patients for personalized therapies.

A significant proportion of patients with lung cancer, however, do not show any of the above genetic abnormalities.

Approximately 90% of lung cancers exhibit RB1 mutation/ deletion and or KRAS mutations, therefore, the signaling pathways, which regulate multistep tumorigenesis in lung cancer, are important for the treatment of histologic subtypes of lung cancer, which includes NSCLC & SCLC. Equally important was the findings that similar signaling pathways are also shared by other solid tumor types.

We have investigated the role of these pathways to target these cancers and develop new strategies to treat lung, brain and related cancers. In addition, our translational studies in other tumor types such as NF2 related malignancies, Specifically, Malignant Mesothelioma (MM), in which NF2 related pathway amenable to targeted therapies was identified. Selected examples representing of these tumor types will be discussed to illustrate the critical role of translational research in developing novel therapeutic approaches for the successful and durable responses in some of these cancer types.

Artificial Intelligence in Thoracic Surgery

Akif Turna

Istanbul University-Cerrahpaşa Cerrahpaşa Medical Faculty Department of Thoracic Surgery

Artificial intelligence (AI) is defined as a branch of computer science that uses computational models to perform tasks that previously required human intelligence. It is increasingly being applied across various areas of thoracic surgery, offering new possibilities for diagnosis, treatment, and patient management. The concept of AI dates back to Ada Lovelace, often regarded as the first computer programmer, who wrote an algorithm for the 'Difference Engine 'and stated that "a machine can do whatever we know how to order it to do."

There are several areas of AI:

1. **Machine Learning**: Training computer programs to recognize patterns in data using algorithms.
2. **Neural Networks**: Computer systems that mimic the behavior of neurons in the brain.
3. **Natural Language Processing (NLP)**: The ability to process and analyze human speech and text.
4. **Robotics**: Machines designed to perform tasks without human intervention.

In thoracic surgery, AI is poised to meet several unmet needs, such as:

- Improved complication prediction
- Prediction of lymph node involvement without invasive procedures
- Early detection of lung cancer, including ground-glass opacities (GGOs)
- Identification of patients who would benefit from targeted therapy or immunotherapy
- Prognosis prediction for resected lung cancer patients
- ICU admission prediction after surgery

One of the earliest uses of AI in thoracic surgery was a study conducted 20 years ago using "fuzzy logic" to predict complications after lung cancer surgery, with an accuracy rate of 76%. This early work laid the foundation for more advanced AI applications in the field.

AI plays an increasingly important role in **preoperative planning** by assisting in the analysis of imaging data like CT scans and MRIs. Algorithms based on Bayes 'theorem have helped estimate the malignancy risk in patients with solitary pulmonary nodules, though accuracy has been a concern. However, AI holds promise for earlier detection of non-small cell lung cancer (NSCLC), which could improve survival rates, as surgical resection of early-stage NSCLC can lead to a 90% five-year survival rate.

AI is also used to predict lymph node metastasis, with algorithms achieving an F1 score of 0.67 using 14 clinical parameters. In a study by Wang et al., convolutional neural networks (CNN) interpreted FDG-PET images with 87.8% specificity and 85.5% sensitivity, compared to 73.9% sensitivity for physicians. Other research by Dercle et al. demonstrated that radiomic signatures could predict overall survival in NSCLC patients, aiding risk stratification in clinical trials.

In postoperative care, AI models have been used to predict ICU admissions, achieving an F1 score of 0.945. AI has also shown promise in predicting responses to anti-PD-L1 treatments, with studies reporting an accuracy of 98% for digital MPR in pathologic response prediction.

The **minimally invasive revolution** in thoracic surgery, driven by techniques like VATS and RATS, has already transformed patient care, and AI is enhancing these advancements. AI has been integrated into robotic-assisted surgeries, such as navigating robotic bronchoscopes through peripheral pulmonary nodes. Additionally, generative AI tools like ChatGPT can assist in clinical note generation, medical image segmentation, multidisciplinary team emulation, and robotic system integration.

However, several challenges remain. AI models are highly data-dependent, and incomplete datasets can reduce accuracy. The "black-box" nature of AI and limited generalizability of algorithms, which are often based on specific datasets, are significant concerns.

Legal frameworks must also adapt to address issues arising from AI use in medical practice. Ultimately, AI algorithms should always be interpreted by humans to mitigate biases and ensure contextual relevance.

Looking forward, the potential of AI in thoracic surgery is vast. It may one day replace multidisciplinary team evaluations, aid decision-making, and even enable fully autonomous surgeries. However, human oversight will remain essential to guide AI in fulfilling its promise in the operating room and beyond.

References

1) Turna A,Mercan CA, Bedirhan MA. Prediction of morbidity after lung resection in patients with lung cancer using fuzzy logic Thorac Cardiovasc Surg 2005 Dec;53(6):368-74.
2) Vaidya YP, Shumway SJ. Artificial intelligence: The future of cardiothoracic surgery. J Thorac Cardiovasc Surg. 2024 Apr 27:S0022-5223(24)00371-4.

3) Jiang, L., Zhou, Y., Miao, W., Zhu, H., Zou, N., Tian, Y., et al. Artificial intelligence-assisted quantitative CT parameters in predicting the degree of risk of solitary pulmonary nodules. *Annals of Medicine*, 2024;*56*(1).
4) Wang, H., Zhou, Z., Li, Y. *et al.* Comparison of machine learning methods for classifying mediastinal lymph node metastasis of non-small cell lung cancer from ^{18}F-FDG PET/CT images. *EJNMMI Res* 2017; **7**, 11 (2017).
5) Dercle, Laurent, et al. "Baseline radiomic signature to estimate overall survival in patients with NSCLC." *Journal of Thoracic Oncology* 18.5 (2023): 587-598.
6) Sanja Dacic, William D. Travis, Jennifer M. Giltnane, Filip Kos, John Abel, Stephanie Hilz, Junya Fujimoto, Lynette Sholl, et al. Artificial Intelligence–Powered Assessment of Pathologic Response to Neoadjuvant Atezolizumab in Patients With NSCLC: Results From the LCMC3 Study. Journal of Thoracic Oncology. 2024; (19):5:719-731:2024.

Systematic Analysis of Genetic Variant Identification and Pathogenicity Prediction

Mehmet Baysan

Istanbul Technical University, Department of Computer Engineering

Recent advancements in sequencing technologies have revolutionized genomic profiling, enabling detailed examination of various genomic features. These technologies primarily utilize short reads that are merged and compared to reference genomes for variant identification. The sheer volume and complexity of the data necessitate computer-based analysis, leading to the development of numerous software programs for mapping, variant calling, and annotation. However, multiple studies have revealed significant discrepancies among popular mapping and variant calling algorithms, highlighting the unreliability of depending on any single algorithm. This underscores the critical need for user-friendly, open-source software tools that facilitate comparative analysis, especially given the rapid growth of sequencing technologies.

To address this need, we present the Comparative Sequencing Analysis Platform (COSAP), an innovative open-source platform designed to streamline and enhance DNA sequencing analysis. COSAP integrates popular sequencing algorithms for single nucleotide variant (SNV), indel, and structural variant calling, alongside copy number variation, microsatellite instability, and fusion analysis. The platform also incorporates annotation capabilities for comprehensive genomic interpretation.

Developed using Python for its core and backend components and React for the frontend, COSAP offers a fully functional, user-friendly web interface coupled with a robust backend server. This architecture enables fully independent deployment, making it suitable for both individual researchers and large-scale institutional use. The platform's modular structure allows for easy customization of pipelines that combine different algorithms and facilitates the integration of new algorithms with minimal coding effort.

COSAP was rigorously validated using the SEQC2 gold standard somatic variants dataset, with pipeline comparisons conducted using VCF Observer. To ensure seamless integration and deployment across various computing environments, all components of the platform are containerized using Docker technology.

The standardized implementation of popular algorithms within COSAP's modular framework provides users with the ability to perform comparative analyses easily. This feature is crucial for assessing the impact of alternative pipelines and establishing the reproducibility of sequencing analyses, which is of paramount importance in genomic research and clinical applications.

By offering a comprehensive suite of commonly used algorithms and a user-friendly interface, COSAP significantly simplifies and accelerates the process of DNA sequencing analysis.

Its ability to handle various types of genomic variations and provide annotations makes it a versatile tool for researchers and clinicians alike. The platform's open-source nature and modular design encourage community contributions and adaptations, fostering continued improvement and expansion of its capabilities.

In conclusion, COSAP represents a significant advancement in genomic analysis tools, addressing the critical need for comparative sequencing analysis in an era of rapidly evolving sequencing technologies. Its user-friendly interface, comprehensive algorithm integration, and flexibility in deployment make it an invaluable resource for the genomics community, contributing to more robust and reproducible sequencing analyses across various research and clinical applications.

Fundamentals and sustainability of Future Science in Medical and Reseach Laboratories

Uzay Görmüş DéGrigo

Karolinska Institutet, Department of Medical Biochemistry and Biophysics, Solna, Sweden

Summary:

Medical laboratories play a crucial role in healthcare and need to be mindfull about the future improvements in the area and about their responsibilities in sustainability of the environment.

In summary, the challenges in the sustainability are;

- Waste Generation: Production of large amounts of hazardous and non-hazardous waste.
- Resource Consumption: High usage of energy and water.
- Greenhouse Gas Emissions: Laboratories are significant contributors to global emissions.

Novel strategies need to be considered for the waste management, energy conservation, using environmentally friendly chemicals and reducing water usage through efficient practices, so holistic approach for balancing environmental sustainability need to be applied. By focusing on these areas, medical laboratories can significantly reduce their environmental impact and contribute to a sustainable future in healthcare. This requires a cultural shift, continuous education, and strong management support.

And in addition to that, the laboratories need to be ready for the upcoming technological transformations. The virtual realities and metaverseconcepts are making waves in various fields, including healthcare and clinical laboratories. We need to be aware of the novelties, for such like below:

- Virtual Medical Consultations
- Medical Education and Training
- Digital Twins: Thee virtual replicas of patients, medical devices, or even entire laboratories which can be used for simulations, monitoring, and improving patient outcomes.
- Clinical Trials: The decentralized clinical trials allowing patients to participate from distance, breaking down geographical barriers and improving patient and researcher engagements.

Epidrug Screening Identifies Type I PRMT Inhibitors as Modulators of Lysosomal Exocytosis and Drug Sensitivity in Cancers

Ceyda Acilan AYHAN[1,2]

[1]Koc University, School of Medicine, Sariyer, 34450, Istanbul, Turkiye

[2] Koç University Research Center for Translational Medicine (KUTTAM), Sariyer, 34450, Istanbul, Turkiye

Epigenetic changes drive differential gene expression, contributing to oncogenic transformation and drug resistance. Lysosomes are crucial in cell signaling and the sequestration of toxins and chemotherapeutic agents. This sequestration followed by expulsion through lysosomal exocytosis is a factor in drug resistance. The epigenetic regulation of lysosomal exocytosis remains poorly understood. Our research focuses on this regulation, hypothesizing that epigenetic modifier drugs (epidrugs) capable of inhibiting lysosomal exocytosis and could serve as potential therapeutics. Additionally, we investigate their potential synergy with drugs known to be sequestered in lysosomes.

To examine this concept, we screened approximately 150 epigenetic drugs targeting various reader, writer, or eraser proteins. These drugs were assessed for their combined cytotoxic effects with cisplatin, their impact on lysosomal exocytosis, and on lysosomal biogenesis. Our findings reveal that among the epidrugs showing synergy with cisplatin and further reducing cell viability in combination, two type I PRMT inhibitors, MS023 and GSK3368715, inhibited lysosomal exocytosis. Notably, neither of these drugs altered the expression of the CLEAR lysosomal biogenesis network of genes, suggesting the involvement of novel regulators in lysosomal functions. To explore the specific components of the trafficking machinery affected by PRMT inhibitors, we conducted an RNA-seq analysis, uncovering several differentially expressed genes (DEGs). In addition to previously described functions such as methylation activity, or DNA repair; these DEGs included those involved in vesicular trafficking, lysosomal enzyme activity and lysosome dynamics, offering potential insights into the mechanism of reduced exocytosis and identifying a novel mode for its regulation. Additionally, both inhibitors exhibited synergy with other drugs known to be sequestered in lysosomes, such as carboplatin, oxaliplatin, sunitinib, and doxorubicin, indicating that inhibition of lysosomal exocytosis may be a common phenomenon for such drugs.

These findings underscore the potential of Type I PRMT inhibitors as therapeutic agents in cancer treatment. Consistently, analysis on the publicly available patient data revealed that lower levels of type I PRMTs (PRMT1 and 6) were associated with better patient response to these drugs, further suggesting their potential as drug candidates for combination therapy to enhance chemotherapy efficacy and improve cancer patient survival rates."

Pharmacological Modulation of Nrf2

Luciano Saso

Faculty of Pharmacy and Medicine, Sapienza University of Rome, Rome, Italy

Oxidative stress (OS) plays an important role in many diseases but very often it is not clear if it is among the causes or the consequences of the pathological conditions. We have to admit that most of the Clinical trials performed with antioxidants failed for different reasons, including the following (Saso and Firuzi, 2014).

In the last two decades, it has become clear that the main *in vivo* mechanism of action of antioxidants is not related to the direct scavenging of free radicals (reactive oxygen, nitrogen

or sulphur species) but to the activation of the nuclear factor erythroid 2-related factor 2 (NRF2), the master regulator of endogenous antioxidant enzymes (Saso et al 2014)

Category	Examples
Michael reaction acceptors	Curcuminoids, cinnamic acid derivatives (caffeic acid phenethyl ester or CAPE, ferulic acid ethyl ester, *etc*.), coumarins, chalcones (sofalcone, isoliquiritigenin, *etc*.), flavonoids (quercetin, fisetin, genistein, *etc*.), triterpenoids (oleanolic acid, bardoxolone methyl, *etc*.), sesquiterpenes (zumberone, *etc*.), citral
Dithiolethiones	Oltipraz, allyl sulfides
Oxidisable diphenols, phenylene diamines, quinones	Butylated hydroxyanisole, butylated hydroxy-toluene, *tert*-butylhydroquinone, resveratrol, epigallocatechin gallate (EGCG), carnosol
Isothiocyanates/ sulfoxythiocarbamates	Sulforaphane, benzylisothiocyanate
Thiocarbamates	Pyrrolidine dithiocarbamate
Polyenes	Lycopene, porphyrins
Dimercaptans	α-Lipoic acid
Selenium-based com-pounds	Ebselen
Hydroperoxides*	Hydrogen peroxide, *tert*-butyl hydroperoxides
Trivalent arsenicals*	Arsenic trioxide
Heavy metals*	Methyl mercury, cadmium, zinc, auranofin

* These agents are not antioxidants, but may activate Nrf2.

Nrf2 is able to eliminate ROS, carcinogens, and many other DNA-damaging agents, which leads to inhibition of tumor initiation and cancer metastasis. On the other hand, increased Nrf2 activity in many cancer types assist malignant cells to defend against excessive oxidative stress, chemotherapeutic agents and radiotherapy and further on avoid apoptosis via activation of cytoprotective genes that contribute to enhanced cell proliferation (Gallorini et al 2023). Thus, inhibitors and not activators of NRF2 should be used in cancer therapy (Telkoparan-Akillilar et al 2021). Some of them are already available but more research is needed to identify the proper therapeutic conditions.

Recently, it has been clarified that NRF2 plays a very significant role not only in the antioxidant response and xenobiotic detoxification but also in the regulation of genes involved in proteosomal and autophagic function, iron, lipid and carbohydrate metabolism and DNA repair. From the pharmacological point of view, the picture is particularly complex because in diabetes and other diseases NRF2 can play a protective or pathogenic role depending on the timing and duration of its activation. Despite the presence of several contradictory publications, in type 2 diabetes, the most common form of diabetes, the activation of NRF2 before the development of diabetic outcomes seems to be beneficial.

However direct electrophilic activators of NRF2 can have several off-target effects and better drugs capable of disrupting the NRF2-KEAP1 binding should be developed.

In conclusion, NRF2 is an important pharmacological target and the development of better modulators of this pathway could be beneficial for the treatment of cancer, neurodegenerative diseases, diabetes and metabolic diseases.

Selected references

Firuzi O, Miri R, Tavakkoli M, Saso L. Antioxidant therapy: current status and future prospects. Curr Med Chem. 2011;18(25):3871-88. doi: 10.2174/092986711803414368. PMID: 21824100.

Gallorini M, Carradori S, Panieri E, Sova M, Saso L. Modulation of NRF2: Biological Dualism in Cancer, Targets and Possible Therapeutic Applications. Antioxid Redox Signal. 2024 Apr;40(10-12):636-662. doi: 10.1089/ars.2022.0213. Epub 2023 Sep 6. PMID: 37470218.

Saso L and Firuzi O. Pharmacological Applications of Antioxidants: Lights and Shadows (Curr Drug Targets. 2014;15:1177-99)

Telkoparan-Akillilar P, Panieri E, Cevik D, Suzen S, Saso L. Therapeutic Targeting of the NRF2 Signaling Pathway in Cancer. Molecules. 2021 Mar 5;26(5):1417. doi: 10.3390/molecules26051417. PMID: 33808001; PMCID: PMC7961421.

Targeting of Oncogenic Pathways by Natural Products: Underlying Mechanisms and Proof-of Concept Animal Model Studies

Ammad Ahmad Farooqi

Institute of Biomedical and Genetic Engineering (IBGE)- Pakistan

Natural product research has spanned over a millennia and interdisciplinary researchers have witnessed ground-breaking discoveries in the identification of pharmacological and medicinal significance of bioactive molecules from natural sources. Because of amazing proof-of-concept studies and exponential increase in the list of natural products having significant properties in the treatment and management of diseases. Two Nobel prizes related to Artemisinin and capsaicin have glorified the field of natural product research and high-throughput technologies have revolutionized the facet of translational medicine. Molecular oncology is a multi-disciplinary field and therefore, basic, applied and clinical researchers have generated high-quality scientific evidence about the underlying mechanisms and targeting of oncogenic pathways.

Nano-solutions for Big Problems: Targeted Drug Delivery Systems

Mükerrem Betül Yerer Aycan

Erciyes Univertsity, Faculty of Pharmacy, Dept. of Pharmacology, Drug Application and Research Center (ERFARMA), Kayseri, Turkiye

Drug Delivery Systems are in deep interest of the researchers for the last decades. The aim of the drug delivery systems are to target the molecular basis of the disease pathology. Therefore, many drug delivery sistems are firstly focused on increasing the bioavailability of the drugs which cannot reach the the active side of the molecule and secondly to target the responsible molecules within the disease pathology are the main goals of these delivery systems. For the drug delivery, there are many methods using the nanotechnology including the lipid-based, carbohydrate-based, protein-based and polimer-based nanoformulations. Among these targeted drug delivery systems the most frequently drugs are basically focuces on cancer. Targeted therapy works by targeting the cancer's specific genes, proteins, or the tissue environment that contributes to cancer growth and survival. These genes and proteins are found in cancer cells or in cells related to cancer growth and micro environment. The U.S. Food and Drug Administration (FDA) has approved targeted therapies for many types of diseases including cancer and there are several types of them: Drugs called "monoclonal antibodies" block a specific target on the outside of cancer cells and/or the target might be in the area around the cancer. Drugs called "small-molecule drugs" can block the process that helps cancer cells multiply and spread which includes the angiogenesis inhibitors. All these targeted molecules and nanoformulations has opened a new era in personalized medicine in many diseases and are important for the novel drug discovery.

Biopolymer Based Nanoparticles for Metabolic Diseases

Burcu Okutucu

Ege University, Faculty of Science, Biochemistry Department, 35100 Bornova, İZMİR

The metabolic disorders can be the dysregulation of glucose, lipids, and some problems about mitochondria. The energy-producing mitochondria in metabolic disorders contributes to redox imbalance and cellular dysfunction, leading to dysfunctional cells and tissues. The metabolic disease, such as hypertension, various types of cancer, cardiovascular diseases, ischemia, and reproductive abnormality are the results of this dysfunctionality.

Nanomaterials are successfully addressing these challenges by finding new ways for potential treatment, intending to overcome the obstacles of conventional treatment forms. Nanomedicine exploited the application of nanotechnology to deliver diagnostic and therapeutic agents for imaging and therapeutic purposes via nanocarriers with a size range of 1–1000 nm. These nanocarriers have been extensively explored to provide efficient tools for diagnostic and therapeutic applications, especially for cancer imaging and targeted therapy, reasonably due to their small size, easy modification and functionalization, enhanced permeation and retention (EPR) effect, superior cellular uptake, as well as good biocompatibility. There are various nanomedicine systems that are existing or being developed for the diagnosis and treatment of these diseases. The polymers (natural/ synthetic) paramagnetic nanoparticles (NPs), quantum dots (QDs), gold NPs, solid lipid NPs, polymeric micelles, fullerene-based derivatives, carbon nanotubes, dendrimers, nanopores, exosomes and liposomes are some of examples. The polymer-based nanoparticles drug delivery system stands out for its many benefits, such as its surface functionalization, high payload, and ability to protect loaded therapeutic molecules from biological barriers.

Drugs used in the polymer-based delivery strategy can also be easily coated with other substances, prolong drug retention, resulting in the smooth release of drugs once they reach their target. The capacity to connect to a specific cell is greatly improved by surface functionalization. The surface functionalization of NPs can increase their therapeutic efficacy by facilitating their internalization and release from cells.

The protein, carbohydrate, nucleic acid and lipid based nanoparticles which are used in biomedical area have many advantages but reasons for the low bench-to-bedside translation of these cancer nanoparticles based nanomedicines lie in various aspect the genetic heterogeneity results in the complexity of cancers, which may lead to totally different responses of the nanotherapeutics. The biological destinies of NPs also can be significantly affected by their physical properties (e.g., size, geometry, composition, surface features, and targeting ligands). The low stability during storage (especially for nucleic acid-based nanodrugs) or complicated manufacturing procedures of NPs can also hinder their clinical applications and many others.

Multifunctional Bioactive Peptides for Cancer Diagnosis and Therapy

Figen Zihnioglu

Ege University, Faculty of Science, Biochemistry Department, Bornova/Izmir/Turkiye

Multifunctional bioactive peptides have emerged as a promising frontier in cancer diagnosis and therapy due to their unique biochemical properties and multifaceted applications. These peptides possess the ability to selectively target cancer cells, penetrate tumor tissues, and deliver therapeutic agents with high specificity and minimal toxicity. Their small size, stability, and ability to modulate a range of biological processes make them ideal candidates for both diagnostic imaging and targeted drug delivery. Recent advancements in peptide engineering have led to the development of peptides that can simultaneously perform multiple functions, such as imaging, targeting, and therapeutic intervention.

Anticancer peptides (ACPs) are a subset of host defense peptides, also known as antimicrobial peptides, which come out as therapeutic and diagnostic candidates due to several advantages over the non-specificity of current routine treatments. ACPs are typically short peptides that can inhibit tumor cell proliferation or migration, suppress the formation of tumor blood vessels, and are less likely to cause drug resistance. Structurally, ACPs' amphipathic/cationic nature allows them to interact with and disrupt the lipid membranes of cancer cells, leading to cell death. Additionally, many ACPs contain cyclic structures with disulfide bonds, which enhance their stability and resistance to proteolytic degradation.

In cancer diagnosis, bioactive peptides can be conjugated with imaging agents to enhance the visualization of tumors, enabling more accurate detection and staging. For example, peptides derived from marine sources have shown potential in inhibiting tumor growth and metastasis. These peptides exhibit a natural affinity for cancer cells, allowing for precise targeting and reduced off-target effects. Such specificity enhances the accuracy of diagnostic imaging, leading to better treatment planning and monitoring. Therapeutically, multifunctional peptides can be designed to interfere with critical pathways in cancer cell growth and survival. They can deliver cytotoxic drugs directly to tumor cells, thereby increasing the efficacy of the treatment while minimizing systemic toxicity. Additionally, these peptides can modulate the immune response to enhance the body's own ability to fight cancer. This immunomodulatory effect is particularly valuable in combination therapies, where peptides work synergistically with other treatments to improve overall outcomes.

Moreover, multifunctional peptides can be engineered to respond to specific conditions within the tumor microenvironment. For instance, peptides that are activated by acidic pH or overexpressed enzymes in the tumor milieu ensure that their therapeutic action is localized to the tumor site, thus reducing systemic side effects. This targeted approach not only improves the therapeutic index but also minimizes damage to healthy tissues. By utilizing the unique features of multifunctional bioactive peptides, current research focuses on to create more effective and personalized cancer treatments that improve patient outcomes and quality of life.

Fusion Analyzes and Clinical Significance in Next-Generation Sequencing in Tumor Tissue

Safiye Aktas

Dokuz Eylül University, Institute of Oncology, İzmir, Turkiye

Gene fusions have a pivotal role in cancer precision medicine. Fluorescence in situ hybridization (FISH)and immunohistochemistry (IHC), RT-PCR. NGS panels are available. The analysis can be performed at DNA or RNA levels. Gene fusion testing presents more technical challenges than other variants. Different target enrichment (hybrid-capture or amplicon-based) and sequencing chemistries are used. Both custom and commercially panels are available.

FISH detects gene rearrangements at DNA level; it is mainly based on the use of break apart probes and does not require knowledge of the fusion partner. In many cases it is considered the gold standard and can discriminate rearrangements from polysomy and amplification, but it does not allow a determination of the exact fusion variant. Break apart probes can miss small intrachromosomal rearrangements and not all the identified DNA rearrangements produce an expressed fusion transcript.

IHC detects fusion proteins, besides the specific fusion variant: whenever an in-frame rearrangement occurs, the 3-prime region of the oncogene is juxtaposed with the 5-prime sequence of a fusion partner gene highly expressed in tumor cells, leading to an active and expressed oncoprotein. IHC has a good sensitivity, almost all molecular pathology laboratories are familiar with this method, it is time saving and also easily automatable, cost-friendly, and different clinically validated antibodies are available. Treatment decisions can be made when ALK IHC results are clearly positive, whereas positive ROS1 and NTRK IHC results have to be confirmed. Although multiplexing has been improved, FISH and IHC usually require a test for each gene to analyze, expert pathologists are needed and results can be influenced by interobserver variation.

RT-PCR allows a highly sensitive detection of fusion transcripts at RNA levels, but it requires primer pairs specific for the known fusion to investigate. This approach suffers from RNA quality, which is often poor from formalin-fixed and paraffin-embedded (FFPE) samples, allows the analysis of few variants at time and misses all the unknown variants.

RNA-based targeted approach analyses and quantifies directly fusion transcripts and is more accurate than DNA panels on tumor tissue. The method is limited by RNA quality and quantity. On liquid biopsy, satisfying data have been published on circulating tumor DNA hybrid-capture panels. There is not a perfect method for gene fusion analysis, but NGS

approaches, though still needing a complete standardization and optimization, present several advantages for the clinical practice. DNA sequencing evaluates different alteration types simultaneously, but large introns and repetitive sequences can impact on the performance and it does not discriminate between expressed and unexpressed gene fusions. Fusion genes are hybrid genes generated by the juxtaposition of two previously independent genes, following structural rearrangements like deletions, inversions, translocations or duplications within the same chromosome or between different chromosomes. Currently, more than 10,000 gene fusions have been identified in human cancers, many of which are strong driver alterations.

There is not a perfect method for gene fusion analysis, but NGS approaches, though still needing a complete standardization and optimization, present several advantages for the clinical practice.

References

Bruno R, Fontanini G. Next Generation Sequencing for Gene Fusion Analysis in Lung Cancer: A Literature Review. Diagnostics (Basel). 2020 Jul 27;10(8):521. doi: 10.3390/diagnostics10080521.

Gatalica, Z., Xiu, J., Swensen, J. et al. Molecular characterization of cancers with NTRK gene fusions. Mod Pathol 32, 147–153 (2019).

A Novel Approach to Drug Resistance in Cancer: Ferroptosis

Güliz Armagan

Ege University, Faculty of Pharmacy, Department of Biochemistry, Izmir, Turkiye

Historically, cell death has been classified into three main types, each characterized by distinct morphological features. Among these cell death types, regulated cell death was once thought to be synonymous with apoptosis. However, recent findings have revealed that there are multiple forms of regulated cell death having spesific molecular mechanisms. Thus, morphologic classification of cell death was replaced with a new classification based on molecular events and biochemical mechanisms. A novel form of programmed cell death, ferroptosis, was identified in 2012. It is characterized by morphologically intact cell membrane, accumulation of redox active iron and lipid peroxidation products, and decreased glutathione peroxidase-4 (GPX4) activity.

During tumor development, cancer cells can undergo various regulated forms of cell death including apoptosis, autophagy and necrosis. Unsurprisingly, ferroptosis also plays a role in the development of cancer. It has been shown that factors such as iron accumulation or fatty acid synthesis enable tumor growth in cancer (pancreatic cancer, breast cancer, melanoma etc.) but they also increase the susceptibility to ferroptotic cell death. Studies have shown that small molecules can induce ferroptosis by inhibiting tumor growth and enhancing the sensitivity of chemotherapeutic drugs. As GPX4 enzyme is a central regulator of ferroptosis-triggering mechanisms, high levels of GPX4 detected in breast cancer support the targetability of ferroptosis.

Carbonic anhydrase IX (CA IX) protects cancer cells against ferroptosis in hypoxic conditions. Reaching of anticancer drugs into tumor cells with an acidic environment is difficult. On contrary, taurinamidobenzenesulfonamide derivatives are able to reach the hypoxic tumor microenvironment due to their acidic primary sulfonamide group. In our laboratory, newly synthesized taurinamidobenzenesulfonamide derivatives which have been reported to show selective CAIX /CAXII activity are evaluated as ferroptotic agents in triple negative breast cancer cell lines (MDA-MB-231, 4T1) in both normoxic and hypoxic conditions.

According to our findings, these derivatives exhibit dose-dependent cytotoxicity in breast cancer cells and affect GPX4-GSH metabolism in hypoxic conditions. It is well known that malignant cells use oncogenic and survival signaling pathways that predispose to ferroptosis. Therefore, induction of ferroptosis by promising compounds is effective and efficient strategy particularly in apoptosis-resistant cells, and may have a future role in cancer therapy.

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Wound Age Determination in the Perspective of Forensic Biology

Yasemin SOYSAL

Dokuz Eylül University, Institute of Health Sciences, Department of Molecular Medicine, İzmir-Turkiye

Wound is described as any damage effecting the integrity of the skin, mucous membrane and organ tissue. Muscles, nerves and blood vessels were involved in complex wounds and mechanical, thermal, chemical or radiogenic sources can create traumatic wounds. In medicolegal case wounds can be grouped by the way that wounds happened as mechanical, physical, chemical, biological. Some questions have to be answered about wound in medicolegal cases as anatomical location of the wound, the nature of the trauma that created the wound, what kind of object was it created with? wounds individual characteristics and numbers, injury time, severity of injury. Wound age estimation is an important issue in forensic pathology.

In this content accurate injury time is still challenging and distinction between vital skin wounds and skin alterations occuring after death is a crucial goal. It is necessary to discriminate antemortem wounds from postmortem damage to evaluate the causal relationship between death and any wouns. Moreover, in medicolegal case when the wound is vital, how long before death was sustained is needed to be known. Punishment in legal period effected from the timing and order of wound in multiple traumas. In violant deaths, injury time was important if it was caused while the individula was alive or death. Another issue is the survival time of victim after the wound was occured. Mainly immunohistochemical techniques were used to explore the role of extracellular matrices, adhesion molecules, inflammatory cytokines and growth factors for wound age estimation. Macroscobic findings were used for histopathological examinations. Phase-wise healing starts immediately after injury in three phases inflammatory, proliferative, maturation. Collagens, fibroblast, myofibroblast, fibronectin, adhesion molecules, inflammatory cytokines, chemokines, angiogenic cytokines, transforming growth factor and stress proteins were factors that involved in wound healing process. Collagens are the main extracellular component of the skin and Collagen III can be detected as early as 2-3 days untill 6 days. Fibronectin is the earliest detectable marker, it can be detected in 10 to 20 minutes time immunohistochemically. P-selectin, E-selectin are early markers usable in a few minutes and 1 hour until 7 days in inflammatory phase. Cytokines and chemokines IL-1α, IL-8, MCP-1, MIP-1α protein up-regulation and mRNA levels were showed experimentaly at injury sites making them useful marker. VEGF and TGF- α gene expression were enhanced after injury. Heat shock protein family member Ubiquitin positive ratio considerably exceeding 30%, possibly indicates a wound age of 7-14 days. Oxygen-regulated protein (ORP)-150 is a stress protein and induced under hypoxic conditions. Immunohistochemical and morphometrical anaysis of ORP-150 in the brain may be useful to determine the duration of brain ischemia before death in forensic

autopsy cases. miRNAs are another marker group used for post-mortem examination of wounds and combination of miRNAs with other markers could increase the sensitivity and specificity of wound age estimation.

As a result; in forensic practice the use of immunohistochemical markers is controversial and it is essential to establish standardized diagnostic criteria because a uniform postmortem diagnostic protocol for identifying wound vitality has not yet been proposed.

Key words: Forensic, wound, wound age estimation, marker, postmortem interval estimation

New Insight into Lung Function Using Novel Contrast MR: from Anatomical to Molecular Imaging

Ozkan DOGANAY

Department of Basic Oncology, Health Science Institute, Ege University, 35030, Izmir, Turkiye

Lung diseases including COPD, Asthma, lung cancer, ILD, cystic fibrosis are currently the fourth largest contributor to mortality, and incidences are likely expected to increase in the future according to World Health Organization (WHO) World Health Statistics 2021. Since the coronavirus pandemic has begun in December 2019, researchers and governments paid more attention and realized the need for novel clinical, anatomical and functional lung imaging modalities worldwide. To date, lung imaging conventionally performed using ionizing x-ray technology dates back as far as the 1900s. In fact, the X-ray technology is still serviceable in most of the hospitals after seeing many iterations, it does not meet today's needs for functional, and volumetric imaging of lungs and insensitivity to ventilation and gas exchange abnormalities due to COPD, asthma, lung cancer, ILD, cystic fibrosis, etc. The Computed Tomography (CT) is the second most common lung imaging modality that employs a relatively newer technology for anatomical and volumetric imaging of lungs with a very high spatial and temporal resolution however it is not capable of diagnosing the lung functions including the gas-ventilation and gas-exchange. Although the recent numerical modeling studies with CT imaging are promising for predicting ventilation disorders, they depend on course assumption and statistically are not very reliable for the use of routine clinical practice.

The novel hyperpolarized Xenon-129 (^{129}Xe) gas magnetic resonance imaging (MRI) developed in the 2000s for functional and anatomical imaging of lung diseases in research and just beginning to take hold in the clinic. Hyperpolarized ^{129}Xe MRI provides an increasingly useful imaging technology in pulmonary diseases including COPD, asthma, bronchiectasis, and more recently idiopathic pulmonary disease. Moreover, hyperpolarized ^{129}Xe can be used to measure microstructural changes and emphysematous degenerations of the alveoli and airways through an apparent diffusion coefficient. MR imaging of Hyperpolarized ^{129}Xe gas is safe and well-tolerated with the patient for repeated scans (i.e. longitudinal studies) and particularly useful for drug efficacy, disease pathway investigation, and routine scans even in healthy subjects, children, and sensitive patients. The signal improvement of the lung ventilation volume including trachea, sub bronchi, and alveolar air sacs is of a factor of 10000 compared to the conventional proton MRI.

Although Hyperpolarized ^{129}Xe MRI has been developed for visualization and quantification of abnormal pulmonary ventilation, it provides unique information for the assessment of gas transfer from the alveoli air sacs to the pulmonary tissue and the blood plasma due to the solubility of ^{129}Xe, which behaves in a similar fashion to the diffusion of oxygen in lungs [17-23]. In addition to the quantification of ventilation defects and high-temporal and high-spatial resolutions, hyperpolarized ^{129}Xe spectroscopy techniques are also sensitive to gas-exchange dynamics between the alveolar air sacs, pulmonary tissues, and capillaries, separately and simultaneously. This chemical shift in the dissolved phases would be a promising contrast agent for molecular imaging of lungs providing additional metabolic information about the lungs without using ionizing radiation.

Osteoporosis Treatment via Wnt Signaling Pathway

Aylin Sepici Dincel

Department of Medical Biochemistry, Faculty of Medicine, University of Gazi, Ankara, Turkiye

Bone metabolism is a dynamic process related to the alteration of specific circulating metabolites that can be associated with bone mineral density (BMD). The decreased BMD and deterioration of bone microarchitecture can define osteoporosis. In 2024, a guideline called "Recommendations for the optimal use of bone-forming agents in osteoporosis" was published and commented on anabolic therapies as first-line therapies due to their ability to stimulate new bone formation and improve bone microarchitecture, offering significant benefits in rapid fracture reduction over antiresorptive therapies. Anabolic therapies are part of bone-forming agents, essential in managing osteoporosis, particularly for patients at high risk of fractures. In daily practice, with the use of a limited period, an anabolic agent, romosozumab, which is a humanized monoclonal antibody sclerostin inhibitor, shows a rapid increase in bone formation with a decrease in bone resorption at about three months. Nowadays, the role of the Wnt/beta-catenin pathway and its inhibitors in bone-related disease is a challenging topic as a new approach that is based on our understanding of bone physiology. The wnt/β-catenin pathway plays a major role in the regulation of bone homeostasis. It is important in mediating the signal that couples bone formation with resorption primarily by regulating cell growth, differentiation, and apoptosis. The extracellular Wnt antagonists (sclerostin and dickkopf-1; DKK1) regulate bone formation by binding directly to Wnt ligands or by competing with Wnt ligands for binding to the co-receptors lipoprotein-related proteins 5 and 6 expressed on the surface of bone cells. These inhibitors are expressed and secreted within the bone microenvironment and regulate bone formation and resorption, resulting in changes in bone mass. The topic related to the local use of the therapeutic composition of sclerostin and DKK1 antibodies to support early bone formation and dual inhibition of both proteins secreted within the bone microenvironment may enhance the potential bone formation. Besides increasing osseointegration, accelerating healing and bone volume augmentation in filling insufficient bone sites is another challenging issue.

Taken together, research about the clinical utility of sclerostin and DKK1 antibodies is currently very limited, and more research is highly demanded.

Plasma Sphingolipidomic Profile in Insulin Resistance and Diabetic Dyslipidemia

Mutay Aslan

Department of Medical Biochemistry, Akdeniz University Medical Faculty, 07070 Antalya, Turkiye

Changes in the metabolism of sphingomyelins (SM) have been associated with obesity. Patients with obese type 2 diabetes (T2DM) have increased plasma ceramides (CER), and this increase is associated with insulin resistance and the degree of inflammation. A persistent CER elevation results in excessive ceramide deposition in the muscles of obese individuals with T2DM. Ceramide accumulation in human tissues inhibits insulin action and subsequent glucose uptake through inactivation of protein kinase B (PKB), also known as Akt. The production of metabolites such as ceramide-1-phosphate (C1P), sphingosine and sphingosine-1-phosphate (S1P), which are important regulators of inflammation, have also been associated with an increase in CERs.

Plasma sphingomyelins and ceramides are elevated in obese dyslipidemic T2DM patients. Serum long chain CERs, C24:C16 SM, C24:C16 CER ratio may serve as prognostic and diagnostic markers in type 2 diabetic dyslipidemia.

Key words: sphingolipid, obesity, dyslipidemia, type 2 diabetes.

Introduction

The hallmarks of type 2 diabetes are hyperglycemia and insulin resistance (1-5). Insulin resistance contributes to the characteristic dyslipidemia associated with type 2 diabetes (5-7). The dyslipidemia associated with insulin resistance is also referred to as atherogenic dyslipidemia. Diabetic dyslipidemia is characterized by increased triglyceride, VLDL, IDL, apoB 100 levels; decreased HDL levels (8-10). Type 2 diabetic patients have small HDL particles which are triglyceride-rich (10-13). The aim of the presentation is to discuss levels of SMs and CERs in the circulation of obese patients undergoing LSG preoperatively, at day 1 and at day 30 after surgery. We also examined the relationship between plasma ceramide levels and insulin resistance. Circulating N-SMase activity, C1P and S1P levels were also measured at all time points.

Results and Discussion

We have reported a significant decrease in serum levels of very-long-chain C24 SM, very-long-chain C22-C24 CERs, insulin resistance (HOMA IR) and C1P in obese patients following laparoscopic sleeve gastrectomy (LSG) after postoperative day 1 and day 30 compared to preoperative levels. At 30 days post-surgery, mean body mass index (BMI) was reduced by 11%, fasting triglycerides were significantly decreased, and insulin sensitivity was increased compared to presurgery values. A significant positive correlation was found between

HOMA-IR and serum levels of C22-C24 CERs in LSG patients (14).

In a seperate study we have found that C16-C24 SM, C16-C24 CER and C16 CER-1P levels were significantly increased in T2DM patients with LDL-C above 160 mg/dL compared to those with LDL-C below 100 mg/dL. **C16-C24 SM,** C22-C24 CER, C16 CER and C16 CER-1P levels showed a statistically significant increase in T2DM patients with non HDL-C above 130 mg/dL compared to those with non HDL-C below 130 mg/dL. C24:C16 SM and C24:C16 CER ratio showed a significant correlation with both LDL-C and non HDL-C levels (15).

Restoration of insulin sensitivity and reduction in secondary complications highlight one of the most important benefits of LSG. It is likely that the decreased long-chain CER levels following LSG contribute to the rapid reduction of insulin resistance seen after surgery. Ceramide levels may be an important mediator for insulin sensitivity and inflammation in peripheral tissues.

References

1. Nianogo RA, Arah OA. Forecasting Obesity and Type 2 Diabetes Incidence and Burden: The ViLA-Obesity Simulation Model. Front Public Health. 2022 Apr 5;10:818816. doi: 10.3389/fpubh.2022.818816. PMID: 35450123; PMCID: PMC9016163.
2. Jocken JW, Goossens GH, Boon H, et al. Insulin-mediated suppression of lipolysis in adipose tissue and skeletal muscle of obese type 2 diabetic men and men with normal glucose tolerance. Diabetologia. 2013;56(10):2255-2265. doi:10.1007/s00125-013-2995-9.
3. Hirano T. Pathophysiology of Diabetic Dyslipidemia. J Atheroscler Thromb. 2018 Sep 1;25(9):771-782. doi: 10.5551/jat.RV17023. Epub 2018 Jul 12. PMID: 29998913; PMCID: PMC6143775.
4. Bitzur R, Cohen H, Kamari Y, Shaish A, Harats D. Triglycerides and HDL cholesterol: stars or second leads in diabetes? Diabetes Care. 2009 Nov;32 Suppl 2(Suppl 2):S373-7. doi: 10.2337/dc09-S343. PMID: 19875584; PMCID: PMC2811435.
5. Einarson TR, Acs A, Ludwig C, Panton UH. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007-2017. Cardiovasc Diabetol. 2018 Jun 8;17(1):83. doi: 10.1186/s12933-018-0728-6. PMID: 29884191; PMCID: PMC5994068.
6. Sone H, Tanaka S, Tanaka S, Iimuro S, Oida K, Yamasaki Y, Oikawa S, Ishibashi S, Katayama S, Ohashi Y, Akanuma Y, Yamada N; Japan Diabetes Complications Study Group. Serum level of triglycerides is a potent risk factor comparable to LDL cholesterol for coronary heart disease in Japanese patients with type 2 diabetes: subanalysis of the Japan Diabetes Complications Study (JDCS). J Clin Endocrinol Metab. 2011 Nov;96(11):3448-56. doi: 10.1210/jc.2011-0622. Epub 2011 Aug 24. PMID: 21865372.

7. Zabielski P, Błachnio-Zabielska AU, Wójcik B, Chabowski A, Górski J. Effect of plasma free fatty acid supply on the rate of ceramide synthesis in different muscle types in the rat. PLoS One. 2017 Nov 2;12(11):e0187136. doi: 10.1371/journal.pone.0187136. PMID: 29095868; PMCID: PMC5667851;
8. Blachnio-Zabielska A, Baranowski M, Zabielski P, Gorski J. Effect of high fat diet enriched with unsaturated and diet rich in saturated fatty acids on sphingolipid metabolism in rat skeletal muscle. J Cell Physiol. 2010 Nov;225(3):786-91. doi: 10.1002/jcp.22283. PMID: 20568228.
9. Hammad SM, Pierce JS, Soodavar F, Smith KJ, Al Gadban MM, Rembiesa B, Klein RL, Hannun YA, Bielawski J, Bielawska A. Blood sphingolipidomics in healthy humans: impact of sample collection methodology. J Lipid Res. 2010 Oct;51(10):3074-87. doi: 10.1194/jlr.D008532. Epub 2010 Jul 21. PMID: 20660127; PMCID: PMC2936747.
10. Ogretmen B, Hannun YA. Biologically active sphingolipids in cancer pathogenesis and treatment. Nat Rev Cancer. 2004 Aug;4(8):604-16. doi: 10.1038/nrc1411. PMID: 15286740.
11. Kasumov T, Solomon TP, Hwang C, Huang H, Haus JM, Zhang R, Kirwan JP. Improved insulin sensitivity after exercise training is linked to reduced plasma C14:0 ceramide in obesity and type 2 diabetes. Obesity (Silver Spring). 2015 Jul;23(7):1414-21. doi: 10.1002/oby.21117. Epub 2015 May 12. PMID: 25966363; PMCID: PMC4482773
12. Borodzicz S, Czarzasta K, Kuch M, Cudnoch-Jedrzejewska A. Sphingolipids in cardiovascular diseases and metabolic disorders. Lipids Health Dis. 2015 Jun 16;14:55. doi: 10.1186/s12944-015-0053-y. PMID: 26076974; PMCID: PMC4470334.
13. Haus JM, Kashyap SR, Kasumov T, Zhang R, Kelly KR, Defronzo RA, Kirwan JP. Plasma ceramides are elevated in obese subjects with type 2 diabetes and correlate with the severity of insulin resistance. Diabetes. 2009 Feb;58(2):337-43. doi: 10.2337/db08-1228. Epub 2008 Nov 13. PMID: 19008343; PMCID: PMC2628606.
14. Özer H, Aslan İ, Oruç MT, Çöpelci Y, Afşar E, Kaya S, Aslan M. Early postoperative changes of sphingomyelins and ceramides after laparoscopic sleeve gastrectomy. Lipids Health Dis. 2018 Nov 24;17(1):269. doi: 10.1186/s12944-018-0917-z. PMID: 30474555; PMCID: PMC6260847
15. Aslan et al., Sphingolipidomic profile and HDL subfractions in obese dyslipidemic type 2 diabetic patients. Prostaglandins Other Lipid Mediat. 2023 Jun;166:106719. doi: 10.1016/j.prostaglandins.2023.106719. Epub 2023 Feb 28. PMID: 36863606.

Cancer Immunotherapy & CAR T Cell

Akkoç Tunç[1,2]., Kılıç Sabriye Senem[1,2].

[1] Department of Pediatric Allergy and Immunology, Faculty of Medicine, Marmara University, Turkiye

[2] Department of Immunology, Faculty of Medicine, Marmara University

Cancer remains a significant global health issue, affecting both adults and children with high morbidity and mortality rates. At the cellular level, cancer development is marked by uncontrolled cell division, resistance to apoptosis, invasion, and metastasis. Under normal conditions, the immune system's physiological role is to identify and control the proliferation of abnormal cells to prevent carcinogenesis. In this context, the immune surveillance mechanism aims to recognize and eliminate cancer cells. According to Macfarlane Burnet's theory from the 1950s, adaptive immune components like CD8+ cytotoxic T lymphocytes, tumor-infiltrating lymphocytes (TILs), and CD4+ Th1 cells establish a crucial line of defense against tumor formation. However, tumor cells have evolved adaptive features, such as antigen loss and rapid proliferation, that help them evade immune responses. Understanding these mechanisms of immune surveillance failure lays the groundwork for developing therapeutic strategies targeting the immune system at various stages of cancer progression.

The concept of activating the immune system in cancer treatment has driven recent advances in immunotherapy, resulting in approaches like immune checkpoint inhibition. One of the cornerstones of immunotherapy, immune checkpoint blockade, allows T cells to overcome suppressive signals within the tumor microenvironment. For example, monoclonal antibodies like the CTLA-4 inhibitor ipilimumab and PD-1 inhibitors nivolumab/pembrolizumab target specific immune checkpoints to strengthen the immune response. These treatments have shown
success, particularly in cancers such as metastatic melanoma and lung cancer. However, due to limitations like high toxicity and restricted application areas, alternative strategies such as normalization immunotherapy have been developed to balance efficacy and safety. Anti-PD therapies, for instance, support immune function with minimal toxicity, facilitating broader clinical use.

CAR-T cell therapy, an innovative immunotherapy approach, has shown promising results in hematologic cancers. CAR-T cells are genetically modified T cells engineered to recognize and destroy tumor-specific antigens via chimeric antigen receptors (CARs) on their surface. First-generation CAR-T cells provided basic antigen recognition and activation through CD3ζ signaling, while second-generation CAR-T cells enhanced T cell activation and durability by adding a costimulatory signal (such as CD28 or 4-1BB). In third-generation CAR-T cells, two costimulatory signals were combined to achieve a more sustained response. Fourth-

generation CAR-T cells incorporated cytokines like IL-12 to stimulate a more robust immune response in the tumor microenvironment. Fifth-generation CAR-T cells include an additional signaling element (IL-2Rβ), which activates the JAK/STAT pathway, boosting T cell proliferation and antitumor activity. This evolution across CAR-T cell generations has optimized their success in hematologic cancers and paved the way for new-generation cell therapies.

Despite the success of CAR-T cell therapy, specific limitations persist, especially in solid tumors. The solid tumor microenvironment, enriched with immunosuppressive cells such as fibroblasts and dendritic cells, releases cytokines like TGF-β and IL-10, which hinder CAR-T cell efficacy. Additionally, cytokine release syndrome (CRS) is a common side effect of CAR-T cell therapy; this systemic inflammatory response, driven by excessive production of pro-inflammatory cytokines like IL-6 and IFN-γ, results in severe inflammatory reactions. These limitations necessitate new strategies to enhance CAR-T cell infiltration and antitumor activity in solid tumors. Consequently, research has intensified on combining CAR therapies with other immunotherapies and immune-microenvironment-targeting drugs. Enhancing CAR-T cells' specificity to tumor-specific antigens also remains a key area of investigation.

To overcome the limitations of CAR-T cells in solid tumors, CAR-NK and CAR-macrophage (CAR-M) cell therapies have emerged as promising alternatives. CAR-NK cells, for instance, do not require HLA compatibility, reducing toxicity risk and supporting large-scale production. These cells can be activated by cytokines like IL-2, IL-15, and IL-12 to recognize tumor cells directly and exert antitumor effects through mechanisms such as antibody-dependent cellular cytotoxicity (ADCC). CAR-M cells, on the other hand, have shown superior tumor infiltration and antigen presentation capabilities, strengthening immune responses through tumor cell phagocytosis. These therapies are advantageous, particularly for solid tumors with invasive and metastatic characteristics, providing a promising alternative to CAR-T cells.

In the coming years, the effectiveness of CAR cell therapies is expected to increase through the development of combination therapies that support immune responses. For instance, immune checkpoint inhibitors and immune modulators are being investigated to improve CAR-T efficacy in solid tumors. Supporting CAR cell function with cytokines like IL-2 and IL-15 also holds potential for more robust modulation of the immune microenvironment, aiming for comprehensive and long-lasting antitumor responses. Integrating CAR-NK and CAR-M cells with the adaptive immune system could provide a broader therapeutic application, offering a promising solution, especially for advanced and treatment-resistant cancers.

In conclusion, cancer immunotherapy and CAR cell therapies represent effective and innovative approaches in cancer treatment. Future optimization of these therapies and the development of combination treatments are expected to yield more successful outcomes, particularly for cancer types that are resistant to conventional treatments, such as solid tumors.

Stem Cell Treatment Approaches for COVID-19 and Possible Viral Pandemics

Nihal KARAKAŞ[1, 2]

[1]Department of Medical Biology, International School of Medicine, Istanbul Medipol University, Istanbul, Turkiye

[2]Institute for Health Sciences and Technologies, İstanbul Medipol University, Istanbul, Turkiye

Stem cell therapies have been applied for several diseases, and mesenchymal stem cells are the mostly utilized stem cell sources for clinical translations. What's more, in preclinical studies, genetically engineered mesenchymal stem cells (MSCs) were used to treat cancers. The idea of using therapeutically modified stem cells using various engineering techniques, provides the advantages of both natural behaviour and gained features of stem cells. Naive MSCs have been reported with therapeutic options also for pulmonary diseases and they are utilized in clinics for pulmonary inflammatory diseases, including acute respiratory distress syndrome and acute lung injury. Based on these approach, the novel pathogenic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing coronavirus disease 2019 (COVID-19) was one of the lethal infections that MSCs were applied for therapeutic inventions. Given that MSCs offer a promising treatment against COVID-19, they are being used against COVID-19 in more than 70 clinical trials with promising findings. However, the potential of using engineered MSCs against COVID-19 and prospective viral pandemics has not been explored yet.

Consequently, perspectives on the functionally modified MSCs that can be developed and harnessed for COVID-19 therapy is provided. Molecular dynamics in MSC infection by SARS-CoV-2 have been discussed. Options to manage the SARS-CoV-2 infection and its variants using various genetic engineering tools to increase the therapeutic efficacy of MSCs are highlighted.

Keywords Mesenchymal stem cells, engineered stem cells, SARS-CoV-2, COVID-19, viral pandemics

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Development of Novel Targeted Bherapeutics for Breast and other aggressive cancers

Bulent Ozpolat

Department of Nanomedicine, Houston Methodist Research Institute, Leader, Innovative Cancer Therapeutics, Methodist Dr. Marry and Roy Neil Cancer Center

Houston, TX 77030, USA

Breast cancer is the most common cancer in women and the second leading cause of cancer related deaths. Triple negative breast cancer (TNBC) is highly aggressive, metastatic and the deadliest and incurable type of breast cancer. Significant heterogeneity with 6 genetically defined subtype has prevented development of targeted therapeutics for TNBC.

The chemotherapy remains as a mainstay treatment, however only 50-70% of the patients can not achieve remission and most patients develop resistance and relapse. To develop highly effective targeted therapeutics and prolong patient survival novel molecular targets needed to be identified. After a decade of research our studies identified novel oncogenic atypical kinase, Elongation Factor-2 kinase (EF2K), as major oncogenic driver in TNBC and validated it as a novel therapeutic target initially in TNBC and later highly aggressive other solid cancers such as, pancreatic, ovarian and lung cancers.

To specifically target, we developed tumor-targeting RNA-based (siRNA and microRNA) nanotherapeutics. MicroRNAs (miRNAs) are non-protein-coding RNA molecules 20–25 nucleotides in length that can suppress the expression of genes that are involved in numerous physiological processes in cells. miRNA dysregulation in cancer cells plays a crucial role in cell proliferation, invasion, metastasis, and angiogenesis, drug resistance tumor growth and progression in a broad range of cancers including breast cancer. Thus, strategies involving either restoring the expression of tumor suppressor miRNAs or inhibiting overexpressed oncogenic miRNAs hold potential for targeted cancer therapies.

We demonstrated that single lipid or albumin-based nanoparticles can effectively deliver EF2K-specific siRNA or microRNAs into TNBC tumors in mice, inhibit EF2K gene and suppresses tumor growth with no toxic or side effects in mice, suggesting that this technology may be used clinical translation to patients for Phase 1 clinical trials. We also developed small molecule EF2K-inhibitors (patented) with significant efficacy.

Overall, our data suggest that Elongation Factor-2 kinase (EF2K) provides an oncogenic driver in TNBC and can serve as an excellent novel therapeutic target in TNBC and later highly aggressive other solid cancers such as, pancreatic, ovarian and lung cancers. Most important EF2K-targted therapeutics are safe and effective and can be translated to clinic for the patients. The talk also discuss focus the current state of targeted therapies and successful development of novel targeted therapeutic such as small molecule inhibitors and RNA (miRNA)-based nanotherapeutics which is considered a novel era of targeted therapeutics in treatment of human cancers and diseases.

Functional Dairy Foods and Microbiota Modulation

Eugenia Bezirtzoglou

Democritus University of Thrace, Faculty of Medicine, Laboratory of Hygiene and Environmental Protection, Alexandroupolis, Greece

Functional foods are foods consumed for specific health purposes, because of their constitution in nutrients or other substances which may confer health benefits action for their host. The history of functional foods can be traced back to the first use of cheese and fermented products, that were well known to the Greeks and Romans who recommended their consumption. The fermentation of dairy foods represents one of the oldest techniques for food preservation.

Introduction of the concept is generally attributed to Nobel Prize recipient Eli Metchnikoff, who in 1907 suggested that the "dependence of the intestinal microbes on the food makes it possible to adopt measures to modify the flora in our bodies and to replace the harmful microbes by useful microbes". Metchnikoff correlated the intake of large quantities of Bulgarian fermented milk with the longevity of the Caucasian people.

Since then, multiple strategies and approaches were created for the development of effective functional foods.

Many functional foods now exist in various countries. Regulatory authorities and legislative frameworks in the different countries diverge their features on functional foods. Japan seems to be the country strongly cognizant and supportive of the public health benefits of functional foods, as more than 200 functional foods are proposed marketed under the FOSHU (Foods for Specialized Health Use) legislation. Accordingly, Food and Drug Administration (FDA) in the USA imposed legislation allowing more than 15 food categories grouping different functional foods.

Through centuries fermented cultures were developed from empiric cultures with beneficial action to artificial cultures with particular beneficial action to artificial probiotic cultures with chosen enteric bacteria and finally, since 2000, genetically selected probiotic therapeutic cultures with reinforced properties stimulated the researcher's interest. One of the most promising areas for the development of functional foods lies in modification of the activity of the gastrointestinal tract by use of probiotics, prebiotics and synbiotics.

The contribution of biotechnology has been very important (a) by selection of new strains, (b) improvement of specific functional properties, (c) nutritional improvement of food, and finally(d) improvement of sensory and textural qualities of the final product.

However, the capital role of functional foods is focused on the stimulation of the host immune system and preservation of the microbial intestinal balance via the "barrier effect'.

Beta-cells in diabetes: new look at the old problem

Danilova Irina, Sokolova Ksenia

Institute of Immunology and Physiology, Ural Branch of the Russian Academy of Science

Relevance: Type 2 diabetes (T2D) is a wide-spread chronically disease, which decreases quality and longevity of people's lives all over the world. Insulin resistance and reduction of pancreatic beta-cells mass and activity are the basic processes, involved in the pathogenesis of T2D. One of the mechanisms reducing mass of beta-cells in T2D is their de- and transdifferentiation under various stressors, including inflammation. Ability to manage the functional identity of islet endocrine cells may provide an effective targeted treatment of T2D, since recovery the beta-cells population may compensate the insulin resistance.

Methodology: Early was demonstrated, that sodium 5-amino-2,3-dihydrophthalazine-1,4-dione (APG) possesses anti-inflammatory properties and contributes to increasing the mass of islet and extra-islet insulin producing cells in rats with experimental diabetes. The aim of the current work was to investigate the functional identity of pancreatic islet endocrine cells in experimental T2D. T2D was modeled by intraperitoneal injections of 110 mg/kg nicotinamide followed by 65 mg/kg streptozotocin in male rats weighted 300-350 g. Animals were randomly divided in 4 groups (in each N = 10): 1) T2D 30 days; 2) T2D 60 days; 3) T2D 30 days + APG; 4) intact. We evaluated levels of fasting plasma glucose and glycated hemoglobin, using biochemistry methods. Level of insulin in blood, TNFα, IFNγ and TGFβ1 in blood and pancreas were measured by ELISA. Insulin+, glucagon+, Ki67+, F4/80+ and CD163+ cells in the pancreatic islets were detected immunohistochemically.

Main results and findings: Administration of APG to rats with experimental T2D reduced the level of glycemia and increased the insulin concentration in blood; decreased the level of IFNγ in blood, TNFα in pancreas and increased the level of TGFβ1 in blood and pancreas; decreased the infiltration of pancreatic acini by F4/80-positive (+) macrophages and increased the number of CD163+ macrophages in all parts of the pancreas: in islets, ducts and acini. Thus, the administration of APG reduced the level of inflammation in the body in general and in the pancreas in particular.

The total quantity of cells in islets did not change. Double immunofluorescent staining of pancreatic tissue for insulin and proliferation marker Ki67 did not reveal changes in the proliferative activity of beta cells either in T2D or after administration of APG. At the same time, in T2D the number of insulin+ cells decreased, the number of glucagon+ cells and cells, simultaneously containing both insulin and glucagon, increased. On the contrary, in APG-treated rats the number of insulin+ cells increased and the number of glucagon+ and insulin+glucagon+ cells decreased.

Conclusions: A decrease in the number of β-cells in T2D may occur due to their transdifferentiation into α-cells caused by inflammation. Administration of APG, reducing the level of inflammation in the pancreas, leads to transdifferentiation of α-cells into β-cells. Thus, the level of inflammation in the islets influences the functional identity of islet endocrine cells.

Keywords: β-cell, α-cell, transdifferentiation, islet regeneration, inflammation, sodium 5-amino-2,3-dihidrophtalazin-1,4-dione, type 2 diabetes, experimental diabetes

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Mediterranean Dietary Patterns and Immunonutrition as potential intervention upon gut microbiome in IBD. Wishful thinking or a vision of the future?

Christina Tsigalou

Faculty of Medicine-Democritus University of Thrace-GREECE

Inflammatory Bowel Diseases IBD are chronic relapsing and remitting inflammatory diseases, affecting digestive track with significant morbidity, reduced quality of life and current treatment strategies rely on immunosuppression-immunomodulation, usage of biologics under certain limitations. Chron's disease and ulcerative colitis are under the influence of genetic, immune and environmental factors.

It is generally accepted that diet may influence IBD risk and disease behavior. Firstly, some components of the diet influence microbiota structure and function with downstream effects on immune activity. –dysbiosis-" cause-effect''. Secondly, dietary components act to alter the structure and permeability of the mucosal barrier, and lastly dietary elements may have direct interactions with components of the immune response.

Dietary components with different mechanisms influence and impact on disease control. The role of diet in the pathogenesis and remission of inflammatory diseases is under research. Studies have demonstrated that the Westernized diet and certain dietary components alter the gut microbiota, intestinal mucosal layer as well as mucosal immunity, which are associated with initiation of IBD. In contrast, some food composition and dietary patterns protect or improve intestinal microbiota and result in IBD remission.

Mediterranean dietary plans based on the pyramid model could be tool to combat inflammation and chronic diseases by exploiting polyphenols, lycopene, ω3 fatty acids, trace elements, minerals and vitamins. Several factors contribute to the loss of immune tolerance and induction of autoimmunity by microorganisms, including molecular mimicry, bystander activation, and viral persistence with or without epitope spreading.

IMMUNONUTRITION refers to the effects that dietary factors can have on different aspects of the immune system as well as the microbiome. Immunonutrition is the maintenance and induction of immune homeostasis with the use of nutritional factors, the so called, immunonutrients. It focuses on four "Is" representing an equal number of systemic responses with regards to: a) Immunity, b) Infection, c) Inflammation and d) Injury probiotics, curcumin, vitamins, Selenium, Zinc and n-3 fatty acids as immunonutrients.

The current literature indicates the beneficial role of probiotics in inducing and maintaining remission in ulcerative colitis, while their role in Crohn's disease is strongly doubted. Their efficacy in ulcerative colitis is also supported for prolonged therapeutic schemes lasting more than 24 weeks, and concurrently, probiotics seem a possible treatment option compared to

mesalazine. More well-designed trials and new, personalized therapeutic strategies are needed to comprehensively understand probiotics' role in inflammatory bowel diseases.

Improved gut immunity by probiotics via production of bacteriocins, defensins, and antimicrobial compounds. There is a nutrition competition between probiotics and the pathogens; probiotics provide better attachment to the gut cells and create a barrier against pathogens.

Probiotics can benefit the inner immunity as follows:

Boosting Immune Cells: Probiotics stimulate the production of immune cells that help defend the body against harmful pathogens. Reducing Inflammation: Research suggests that probiotics can help reduce inflammation throughout the body, which is linked to many chronic diseases. Protecting Against Infections: Probiotics have been shown to help reduce the risk of infections and may even be effective in treating certain types of infections.

Overall, the evidence suggests that MED could be a beneficial dietary approach for IBD prevention and management, warranting further research and consideration in clinical practice.

Among the most robust dietary trials (27 studies) in IBD currently available, certainty of evidence remains very low or low. As more dietary studies become available, the certainty of evidence could improve, thus allowing for more meaningful recommendations for patients.

Genetic Signatures: Revealing Insights into Criminal Profiling and Violence

Itır Tarı Cömert

Fatih Sultan Mehmet Vakıf University, Psychology Department

The intersection of genetics and criminal profiling has emerged as a compelling field of study that seeks to unravel the biological underpinnings of human behavior, particularly in the context of violence and criminality. As researchers delve deeper into the human genome, the potential for identifying genetic signatures associated with violent behavior has sparked both interest and controversy. This essay explores the significance of genetic signatures in criminal profiling, the ethical implications involved, and the broader implications for society.

Genetic signatures refer to specific patterns or markers found within an individual's DNA that may indicate predispositions to certain behaviors or health conditions. Recent advances in genomics have identified various genes associated with aggression and impulsivity, traits often linked with violent behavior. For instance, studies have highlighted the roles of neurotransmitter systems and their genetic variations, such as those affecting serotonin and dopamine levels. These genetic factors, when combined with environmental influences, can create a profile that predicts an individual's likelihood of engaging in violent acts.

The potential application of genetic signatures in criminal profiling offers a new dimension to the justice system. By understanding the biological factors that may contribute to criminal behavior, law enforcement agencies could, theoretically, prioritize rehabilitation strategies over punitive measures for individuals identified as having genetic predispositions to violence. This approach could lead to a more informed criminal justice system that considers the complexities of human behavior.

Moreover, in cold cases or unsolved crimes, advancements in DNA analysis allow for the identification of potential suspects through genetic links. For example, familial DNA searches can reveal genetic connections to known offenders, providing crucial leads in investigations. This has been notably effective in high-profile cases, such as the identification of the Golden State Killer, where complex genetic data played a pivotal role in solving decades-old mysteries.

Despite the promising advancements, the application of genetic profiling in criminal justice raises significant ethical questions. The notion of attributing violent behavior to one's genetic makeup can reinforce deterministic views of human behavior, leading to stigmatization

and discrimination against individuals with certain genetic markers. This could blur the lines between biological predisposition and personal responsibility, raising concerns about the potential misuse of genetic information in legal contexts.

Furthermore, the potential for genetic profiling to be used in preemptive measures poses a slippery slope regarding civil liberties and privacy. The idea of categorizing individuals based on genetic risk factors may lead to wrongful accusations or the unfair targeting of specific populations, particularly marginalized communities, which have historically faced disproportionate scrutiny in the justice system.

The exploration of genetic signatures in relation to violence extends beyond individual cases and challenges societal views on crime and punishment. It compels society to reevaluate the concepts of nature versus nurture and how these factors interplay in shaping behavior. As we gather more data on genetic influences, it becomes imperative to integrate this knowledge with sociological perspectives to foster a comprehensive understanding of criminal behavior.

Programs aimed at education and prevention can benefit from insights gained through genetic research. By tailoring interventions for at-risk individuals based on their genetic predispositions while considering environmental factors, we can work towards reducing the incidence of violence in a more humane and informed manner.

As advancements in genetics illuminate the path toward understanding criminal behavior, the integration of genetic signatures into criminal profiling holds both promise and peril. While there is immense potential to enhance our criminal justice system with informed and compassionate approaches, it is essential to tread carefully in this realm. Ensuring ethical standards and protecting civil liberties must remain paramount as society grapples with the implications of genetic insights in the context of crime and violence. Ultimately, striking a balance between scientific understanding and ethical responsibility will be crucial in shaping the future of criminal profiling and addressing the complexities of human behavior.

Exploring Addiction, Violence and Genetic Insights in Forensic Science

Meryem Ebedi[1,2], Emel Hulya Yukseloglu[1]

[1] Institute of Forensic Sciences and Legal Medicine, Istanbul University-Cerrahpasa, Turkiye

[2] Faculty of Medicine, Cyprus Health and Social Sciences University, Cyprus

The complex interplay between genetic predispositions, addiction, and violent behaviour has garnered significant attention in forensic science. Advances in molecular medicine, particularly in genetics and epigenetics, have paved the way for new understandings of these behaviours and their forensic implications.

Addiction is defined as a chronic, relapsing disorder characterized by compulsive drug-seeking behaviour and the inability to abstain, despite severe consequences. This multifactorial condition involves the brain's reward, motivation, learning, and memory systems. From a genetic perspective, addiction is highly polygenic. Studies involving twins, family investigations, and molecular genetics have highlighted the heritability of addiction. Notably, epigenetic mechanisms such as DNA methylation, histone modifications, and non-coding microRNAs (miRNAs) are now recognized as key mediators of gene-environment interactions, influencing addiction vulnerability. Drugs like alcohol and cocaine can induce long-lasting epigenetic changes, which may be heritable, further complicating the treatment and prevention of addiction.

Cocaine use disorder (CUD) is a pertinent example of addiction, where users experience compulsive drug-seeking and relapses, often after attempted abstinence. Research into CUD pathophysiology has revealed metabolic syndrome, oxidative stress, and altered levels of neurotrophins and inflammatory cytokines, indicating a broad systemic impact. Despite current therapeutic efforts, the relapse rates remain high, prompting the need for more targeted interventions. Epigenetic changes induced by cocaine, including miRNA dysregulation, provide a promising avenue for future therapeutic development.

The genetic underpinnings of violent behaviour have similarly been explored through studies of twin concordance and molecular genetics. Variants in the monoamine oxidase A (MAOA) gene, colloquially known as the "warrior gene," have been linked to increased aggression, especially in individuals exposed to early life stress. The serotonin transporter gene (5-HTT) and dopamine receptor D2 (DRD2) gene are also associated with impulsivity, emotional regulation, and risk-taking behaviours, all of which can contribute to violent or criminal actions. These findings provide crucial insights into the biological roots of violent crime, although they also raise ethical concerns regarding determinism and accountability.

The integration of genetic and epigenetic findings into forensic science opens new possibilities for post-mortem studies, personalized treatment plans, and behavioural analysis.

Genetic profiling has already been applied in criminal investigations to some extent, yet it remains a controversial tool due to ethical concerns surrounding privacy, stigmatization, and potential misuse. As forensic science evolves, interdisciplinary collaboration and robust ethical frameworks are essential to harness the potential of molecular medicine while safeguarding individual rights.

The future of forensic genetics lies in balancing the advancements in genetic technologies with societal and legal considerations. The continued exploration of gene-environment interactions, particularly in the context of addiction and violent behaviour, will be crucial in shaping forensic science's role in criminal justice systems. By addressing both the scientific and ethical challenges, forensic science can offer more precise, reliable, and humane approaches to crime investigation and legal adjudication.

Celebrating Uniqueness: The Power of Forensic Genetics in Individual Identification"

Nazlı Holumen

Forensic Science Specialist

The presentation titled "Celebrating Uniqueness: The Power of Forensic Genetics in Individual Identification" delves into the significant role that forensic genetics plays in identifying individuals, explored under four main titles: Molecular Medicine vs. Forensic Science, Individualization, Routine Casework, and Possible Scenarios & Real-Life. Under the 'Molecular Medicine vs. Forensic Science' title, the similarities and differences between molecular medicine and forensic science are detailed. Both fields utilize genetic material and advanced biotechnological methods, but they serve different purposes. Molecular medicine focuses on diagnosing, treating diseases, and conducting health-related research, while forensic science concentrates on analyzing evidence from crime scenes and managing legal processes using scientific methods to solve crimes and forensic incidents. Forensic genetics is only one of the many disciplines under the forensic science umbrella. While other forensic specialists also work in this field, forensic genetics stands out by utilizing genetic materials to solve forensic cases. The presentation clearly explains how genetic analysis techniques are shared between the two fields, but with different focal points. Forensic genetics plays a crucial role in identifying individuals based on their unique genetic structures. The 'Individualization' section focuses on the core concept of "individualization" in forensic genetics. The uniqueness of every person's DNA sequence serves as a powerful tool in forensic science for identifying individuals. The presentation explains how the genetic structure of individuals is analyzed in forensic genetic testing and how this uniqueness is used to identify individuals by comparing DNA found at crime scenes. The presentation demonstrates how genetic information is used in forensic cases and highlights its impact on the justice system. 'The Routine Casework' section explains how forensic genetics is applied in everyday routine cases. This section illustrates how forensic genetic experts conduct DNA analyses, including the collection, preservation, and analysis of DNA evidence. In addition to this, it emphasizes the use of gold-standard DNA tests (such as PCR-based STR analyses) in routine forensic cases. These tests have wide-ranging applications, from identifying perpetrators in sexual assault cases to confirming identities in murder cases. Furthermore, the presentation touches on emerging genetic methods and technologies (such as microRNA studies) that may be used in routine casework in the future. Lastly, in the 'Possible Scenarios & Real-Life' section, examples of real-life cases where genetic analyses were applied are provided, and various scenarios are discussed, highlighting the impact of forensic genetics in criminal investigations. The power of forensic genetics is demonstrated through real cases, with examples showing how DNA found at crime scenes is collected, analyzed, and used to solve crimes. The integration of technological advancements

into genetic analysis has made DNA sequencing faster and more reliable, enhancing the accuracy of individual identification in forensic investigations. In conclusion, this presentation thoroughly addresses the crucial role of forensic genetics in individual identification, emphasizing its importance in both routine forensic cases and complex criminal investigations. It showcases how genetic analyses contribute to ensuring justice, the power of scientific techniques in individual identification, and how technological advancements in this field have facilitated the resolution of forensic cases.

Unveiling the Genetic Code: Exploring Forensic Science at the DNA Level

Omer Karatas

Institute of Forensic Sciences, Department of Natural and Applied Sciences

Molecular medicine has become a vital area of research in recent years, significantly influencing forensic science. The advancements in forensic genetics offer powerful tools for identifying individuals and resolving complex criminal cases, prompting us to present our findings in this field.

Introduction

Forensic genetics is crucial for solving crimes, identifying victims, and establishing familial relationships. DNA analysis has revolutionized criminal justice, providing investigators with essential evidence for legal proceedings. Key techniques include Short Tandem Repeats (STRs), which are highly polymorphic and require small sample sizes. Established databases, such as CODIS, enhance their effectiveness in criminal investigations, paternity testing, disaster victim identification, and cold cases.

Y-STRs and X-STRs

Y-STRs are instrumental in identifying male lineage, especially in cases like paternity testing and sexual assault investigations where male DNA is involved. However, they have limitations, as they cannot distinguish between male relatives sharing the same Y chromosome.

X-STRs, inherited from both parents, offer insights into complex kinship scenarios, such as half-sibling relationships. They can also aid in identifying female contributors in sexual assault cases and are useful for maternal lineage investigations when combined with mitochondrial DNA (mtDNA) analysis. Additionally, X-STRs contribute to population genetics studies, enhancing our understanding of inheritance patterns across genders.

DNA Profiling and Population Genetics

DNA profiling using STRs significantly improves forensic identification accuracy, leading to robust criminal investigations. The establishment of comprehensive forensic databases allows for effective linking of suspects to crime scenes and resolving cold cases. Our research includes population studies in the Turkish and Bulgarian immigrant populations, revealing previously unseen STRs, thereby enriching the field of DNA profiling.

Mitochondrial DNA in Crime Investigations

Mitochondrial DNA (mtDNA) analysis is invaluable for cases with degraded nuclear DNA, such as ancient remains or severely decomposed samples. Its high copy number makes mtDNA useful for solving cold cases. Our studies on hypervariable regions of mtDNA in the Turkish population have increased discrimination power and revealed disease associations, which could help in suspect elimination during investigations.

In mass disaster situations, forensic DNA analysis plays a critical role in victim identification, helping families find closure amid extensive destruction. Understanding population-specific mtDNA and STR frequencies is essential for effective identification in these challenging scenarios.

miRNAs for Body Fluid Identification

Forensic samples are often limited and degraded, necessitating efficient identification methods. MicroRNAs (miRNAs) serve as promising biomarkers for detecting body fluids. For instance, miR-451A has shown potential in identifying blood presence.

Conclusion

Forensic genetics is continuously evolving, enhancing our ability to solve crimes, identify victims, and comprehend human populations. The intersection of forensic science and molecular medicine opens avenues for innovative solutions. We appreciate the opportunity to share our insights and foster collaboration in these dynamic fields. Thank you for your attention.

Critical Considerations on Preclinical Evaluation of Newly Synthesized Anticancer Compounds

Engin Ulukaya

Istinye University Molecular Cancer Research Unit, Istanbul, Turkiye

Anticancer drug discovery is a long way which consists of mainly two parts, preclinical and clinical phases. The success rate of clinical phase is influenced by the quality of preclinical stages. Classically, one in 10.000 compounds may take a place on the shelves of a pharmacy after spending about 12-14 years of research. To enhance this ratio, the preclinical phase should rely on quality assurance-quaranteed, standardized and well-defined approaches. Although in silico designation of candidate drug molecules reduce the discovery period and seems trendy currently, the conventional methods are still in use. There are many considerations to be careful with. First of all, not all types of the compounds are good candidates for cancer drug development such as reactive molecules, thermal or photo labile molecules (e.g. mustards, acyl halides, α-halo carbonyl compounds, reactive Michael acceptors). High MW pegylated or similarly derivatized agents are also other examples for such compounds. Those compounds are called PAINS (Pan assay interfering compounds). Chemical or metabolic stability of the compounds is to be checked carefully in the first place. These are some examples of physicochemical properties of the compounds. However, mechanism of action studies are of particular importance. On the evaluation of antigrowth effect of any compound, it is desired to look for a spesificity towards certain type of malignancy. Otherwise, killing all kinds of cancer types may be a sign of a poison, rather than a proper anticancer drug. When it comes to the evaluation of mode of cell death, apoptosis-inducers may not be fasinating compounds as apoptotic machinary is known to be disrupted in cancer cells. Therefore, necrosis-inducers could be selected for the next stage, omitting apoptosis or autophagy-inducers. Elucidation of mechanism of action could also be the other tricky aspect. General cytotoxics are sometimes considered that they are at the end of the road. Therefore, efforts on new discoveries on such cytotoxics may be discussed. However, this may be wrong because the combination of targeted therapies with general cytotoxics seems to result in better outcomes, compared to targeted therapy alone or general cytotoxic alone. To me, development of general cytotoxics should carry on in a different approach (e.g. their being packed in a nanopartical). Animal experiments are the next stage before the human clinical phases. In silico and AI seem to replace this part. However, new experimental models are also emerging (e.g. The In Ovo Chick Chorioallantoic Membrane (CAM) Assay). It is a beautiful assay for the evaluation of compounds' antiangiogenic effects.

Advanced Therapeutic Medicinal Product: Advantages and Disadvantages

Metin Kurtoglu

Cartesian Therapeutics, Gaithersburg, Maryland, USA

Advanced therapy medicinal products (ATMPs) are medicines based on genes, tissues or cells, and are divided into three classes: somatic cell therapy, tissue engineering and gene therapy medicinal products for human use. ATMPs offer groundbreaking new opportunities for the treatment of diseases and injuries with complex biological structures. The process of developing well-established ATMPs that offer great hope for a variety of diseases with limited or no treatment options is challenging. One important factor that can affect the quality of most custom-designed ATMPs is the variability of the donor starting material and how the disease state affects the quality of the starting material. Because of these variables, a broad but acceptable product specification is critical. In addition, the potential variability of an ATMP depends on the donor variability as well as the limited stability of the ATMP, storage, transportation and handling conditions of the finished product. Therefore, ATMPs are manufactured in authorized laboratories according to Good Manufacturing Practices (GMP), the process must be well planned and scaled up. One of the important ATMPs, CAR-T cells, is of increasing importance in adoptive immunotherapy, and ATMPs have already achieved exciting results and promise to achieve more in the future.

Metabolic Plasticity and Dormant Status of Cancer Cells

N. Nuray Ulusu [1,2]

[1]Koc University, School of Medicine, Department of Medical Biochemistry, Sariyer, 34450, Istanbul, Turkiye

[2] Koç University Research Center for Translational Medicine (KUTTAM), Sariyer, 34450, Istanbul, Turkiye

There are significant metabolic differences between cancer cells and normal cells. Cancer cells primarily rely on anaerobic glycolysis, the Warburg effect for ATP energy production, even in the presence of oxygen, allowing them to generate energy quickly to support rapid proliferation. In contrast, normal cells predominantly utilize oxidative phosphorylation, a more efficient process for ATP production.

Cancer cells often increase their demand for glucose, fatty acids, and glutamine, enabling them to survive under environmental stress conditions, such as hypoxia or nutrient deprivation. These metabolic differences have important implications for cancer therapy approaches. On the other hand, cancer cells exhibit remarkable adaptability through a phenomenon known as metabolic plasticity. Cancer cells can activate many enzymes in metabolic pathways to promote survival. This adaptability allows them to survive in varying microenvironments and under diverse stress conditions, including nutrient deprivation, hypoxia, and therapeutic interventions. Understanding the mechanisms behind this plasticity, particularly concerning the dormant status of cancer cells, is crucial for developing more effective cancer treatments.

Metabolic plasticity refers to the ability of cancer cells to switch between different metabolic pathways depending on environmental cues. While rapidly proliferating cancer cells predominantly rely on glycolysis for energy production (the Warburg effect), dormant cancer cells often shift to a more energy-efficient oxidative phosphorylation pathway. This switch is crucial for survival in the low-nutrient, low-oxygen conditions typical of certain tumor microenvironments.

Cancer is changing the cellular key metabolism. Alterations in the signaling transduction pathways cause metabolic reprogramming and activation of enzymatic types of machinery, stimulating cellular growth via activating anabolic metabolism. These cellular growth mechanisms contributing to the alteration in cellular energy metabolism would induce tumor population and resistance against the cellular death mechanism, high expression of ABC drug efflux transporter, dormant status, metabolic plasticity, deregulation of tumor-associated antigens (TAAs), proficient DNA repair and escape of cell death mechanisms which confer resistance to standard anti-cancer therapies. Immunosuppressive tumor microenvironment (TME) would also affect the most innovative immunotherapy approaches. One of the key points

in cancer cells can alter drug targets by mutation or reduced expression, upregulation of drug pumps, drug detoxification mechanisms, increased DNA repair mechanisms, reduced cell death mechanisms, and increased cellular proliferation. To solve the anticancer therapy, we need to learn how to play molecular chess against different types of cancer cell molecular reprogramming pathways.

In conclusion, the interplay between metabolic plasticity and the dormant status of cancer cells is a critical area of research with substantial implications for cancer therapy. By elucidating the metabolic adaptations that facilitate dormancy, researchers can develop innovative strategies to eradicate residual disease and prevent relapse. Understanding these mechanisms not only enhances our knowledge of cancer biology but also paves the way for more effective therapeutic interventions.

Non-coding RNAs' role and significance in cancer and NDDs

Ahmad R. Bassiouny

Department of Biochemistry, Faculty of Science, Alexandria University, Alexandria, 21511, Egypt

Long non-coding RNAs (lncRNAs) are emerging as critical regulators in the pathogenesis of both cancer and neurodevelopmental disorders (NDDs). These RNA molecules, despite lacking protein-coding potential, modulate gene expression through various mechanisms, including epigenetic regulation, transcriptional control, and post-transcriptional processing. In cancer, lncRNAs function either as oncogenes, promoting tumorigenesis by activating oncogenic pathways, stabilizing oncogene expression, and facilitating metastasis, or as tumor suppressors, inhibiting cancer progression by repressing oncogenes, inducing apoptosis, and preventing metastasis. The tissue-specific expression and distinct roles of lncRNAs in cancer make them promising diagnostic biomarkers and therapeutic targets.

In neurodevelopmental disorders, lncRNAs are pivotal in regulating brain development, neuronal differentiation, and synaptic plasticity. Dysregulation of lncRNAs has been linked to various NDDs, including autism spectrum disorders and intellectual disabilities, by affecting neurogenesis, synapse formation, and neuroinflammatory responses. Detection of long non-coding RNAs (lncRNAs) in cancer and neurodegenerative diseases is crucial for understanding their roles in disease pathogenesis and identifying potential biomarkers. Several advanced techniques are employed to identify and quantify lncRNAs. RNA sequencing (RNA-Seq) offers comprehensive profiling of lncRNAs, providing both qualitative and quantitative insights. Quantitative PCR (qPCR) and microarray analysis are widely used for the precise quantification and validation of specific lncRNAs. In situ hybridization (ISH) allows for the visualization of lncRNAs within tissue samples, revealing their spatial distribution. Northern blotting, while less commonly used, can confirm the size and presence of lncRNAs. CRISPR-based methods, including CRISPR-Cas13, enable targeted detection and functional analysis of lncRNAs. RNA immunoprecipitation (RIP) identifies lncRNA interactions with RNA-binding proteins, providing insights into their functional roles. Additionally, bioinformatics tools are essential for predicting, annotating, and analyzing lncRNAs from large datasets. Together, these techniques enable the comprehensive detection and study of lncRNAs, advancing our understanding of their significance in cancer and neurodegenerative diseases and paving the way for potential diagnostic and therapeutic applications. Given their involvement in critical biological processes, lncRNAs hold significant potential as biomarkers for early diagnosis and as therapeutic targets for both cancer and NDDs. Understanding the molecular mechanisms by which lncRNAs contribute to these diseases could lead to novel therapeutic strategies, offering hope for improved treatment outcomes.

Long Non-coding RNAs in Cell Death and Survial

Bunyamin Akgul

İzmir Institute of Technology, Department of Molecular Biology and Genetics

Cell survival and cell death is tightly regulated by transcriptional and post-transcriptional gene regulatory networks. Genetic, genomic and biochemical studies have shown that cell survival and cell death are modulated by numerous protein-coding genes. However, recent studies provide evidence that cell fates are controlled by non-protein coding genes as well. Genome annotation studies have revealed that protein-coding exons constitute less than 2% of the human genome while the rest is primarily transcribed into noncoding RNAs (ncRNAs) without any functional open reading frame (ORF) or with very short ORFs. Long noncoding RNAs (lncRNAs) are noncoding transcripts of 200 nt or longer in size. Localized in nucleus, cytoplasm or in extravesicular entities, lncRNAs modulate transcriptional and post-transcriptional gene regulatory mechanisms in cis or trans through interactions with DNA, RNA or proteins. We used transcriptomics approaches to identify differentially expressed lncRNAs in HeLa cells treated with chemotherapeutic drugs, such as cisplatin or doxorubicin. Bioinformatic analyses revealed the differential expression of numerous lncRNAs in different biotypes, such as antisense, intronic or intergenic. Death receptor 5 antisense (DR5-AS) lncRNA is a cisplatin inducible lnRNA whose transient knockdown results in reduction in proliferation and cell cycle arrest in HeLa cells. Its knockdown also sensitizes HeLa cells to treatment with cisplatin. RNA immunoprecipitation assays showed that DR5-AS interacts with the RNA-binding protein CAPRIN1, suggesting the potential role of DR5-AS in stress response. Treatment of HeLa cells with lower doses of drugs, such as doxorubicin, induce quite a distinct expression pattern of lncRNAs, suggesting that cells respond differently under high and low doses of drugs. One interesting type of lncRNAs is intron-derived RNAs mostly with unknown functions. More work is required to identify and functionally characterize lnRNAs that regulate cell survival and cell death.

Impact of the Metabolic Targets on Cancer Treatment Regarding Novel Cancer Death Pathways

Duygu Aydemir [1,2]

[1] School of Medicine, Department of Medical Biochemistry, Koç University, Istanbul, Turkiye

[2] Koç University Research Center for Translational Medicine (KUTTAM), Istanbul, Turkiye

Metabolic reprogramming is a fundamental characteristic of cancer cells, facilitating sustained proliferation, metastasis, and resistance to chemotherapy in a nutrient-deficient microenvironment. Consequently, targeting these metabolic alterations has emerged as a promising strategy for overcoming chemoresistance and treating various cancer types, with extensive research on metabolic inhibitors over the past two decades. Key metabolic pathways, including aerobic glycolysis, the pentose phosphate pathway (PPP), fatty acid synthesis, glutamine metabolism, redox homeostasis, oxidative phosphorylation (OXPHOS), nucleotide metabolism, and mitochondrial function—play critical roles in cancer initiation, progression, metastasis, angiogenesis, chemoresistance, and the modulation of the tumor microenvironment (TME). By applying small molecules and enzyme inhibitors, interventions aimed at these pathways have been shown to activate novel cell death mechanisms such as ferroptosis, parthanatos, NETosis, pyroptosis, necroptosis, and cuproptosis. For example, according to preclinical and clinical studies, statins, including lovastatin and atorvastatin, which inhibit the mevalonate pathway, have demonstrated efficacy in promoting remission in various malignancies, including ovarian cancer, lymphoma, and leukemia. Moreover, extensive investigations have been conducted into inhibitors targeting glycolysis, the PPP, and redox metabolism, specifically hexokinase inhibitors, across multiple cancer types, such as ovarian, prostate, pancreatic, lung, stomach, brain, and colorectal cancers.

These findings underscore the critical role of metabolic reprogramming in cancer biology and the potential of metabolic targeting as a therapeutic approach. Several factors, such as tumor heterogeneity, plasticity, adverse effects, and the interactions between the tumor microenvironment (TME) and the tumor itself, pose significant challenges to the efficacy of metabolic targeting therapies. These complexities often contribute to the unsatisfactory outcomes observed in clinical settings. It is essential to identify more accurate and relevant metabolic targets to enhance the precision and effectiveness of metabolic targeting strategies and better elucidate the intricate metabolic landscape of tumors.

The Role of Autophagy in Tumor Microenvironment

Yunus Akkoc[1,2]

[1]Koç University School of Medicine, Department of Medical Biology, 34450 Istanbul, Turkiye
[2]Koç University Research Center for Translational Medicine (KUTTAM), 34450 Istanbul, Turkiye

Surgical interventions and conventional therapies following early diagnosis may be beneficial for a group of patients. However, we are still losing cancer patients due to late diagnosis, drug resistance and recurrent disease. In an advanced stage, increased mutational burden, clonal selection and cancer cell evolution seem to be the most major obstacles against the current therapeutic strategies. Hence, targeting tumor microenvironment components rather than the cancer cells proposes a great perspective to overcome the above-mentioned cancer cell-associated obstacles. Tumors not only consist of cancerous cells but also harbor several normal-like cell types and non-cellular components. Carcinoma-associated fibroblasts (CAFs), an activated form of tissue-resident fibroblasts, are found predominantly in the tumor stroma. Autophagy is an intracellular degradation and quality control mechanism whose deregulation has been associated with different pathologies including cancer. Recent studies also provided evidence that autophagy plays a critical role in CAF formation, metabolic reprogramming and CAF-cancer cell communication. However, communication and the mechanism of autophagy stimulation in the tumor microenvironment are not fully documented. For this purpose, we first focused on CAFs and their role in tumor microenvironment. We identified a factor called CTF1 (cardiotrophin 1) secreted from cancer cells. Our previous data showed that CTF1 is an activator of autophagy in fibroblasts and breast cancer-derived CAFs. We also discovered that CTF1 acted as an important tumor-derived factor regulating breast cancer cell migration and invasion. In line with these *in vitro* observations, we identified that elevated levels of CTF1 in patient-derived tumors showed a positive correlation with lymph node metastasis. Our current analyses suggested that the autophagic capacity of fibroblasts may determine CTF1-associated CAF formation and fibroblast activation in the tumor microenvironment. Overall, our data revealed that CTF1 is a crucial player in stromal autophagy, fibroblast activation and signaling. Targeting CTF1 might bear great potential to develop novel cancer therapeutics from the perspective of tumor microenvironment.

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ORAL PRESENTATIONS

Oral Presentation-01

Targeting ITGβ3 to Overcome Trastuzumab Resistance in HER2-Positive Breast Cancer: Insights into TGF-β Signaling and Migration

Asiye Busra Boz Er[1], Idris Er[2]

[1]Recep Tayyip Erdogan University, Faculty of Medicine, Department of Medical Biology, Rize/Turkiye
[2]Karadeniz Technical University, Faculty of Medicine, Department of Medical Biology, Trabzon/Turkiye

HER2-positive breast cancer, characterized by the overexpression of HER2, leads to aggressive tumor growth. Trastuzumab has significantly improved outcomes for patients; however, resistance remains a major challenge. Tumor heterogeneity, encompassing genetic, and phenotypic differences within and between tumors, complicates treatment and contributes to drug resistance. Understanding the mechanisms underlying trastuzumab resistance, such as tumor heterogeneity, is crucial for developing effective therapeutic strategies.

This study investigates the role of ITGB3 heterogeneity in trastuzumab resistance, focusing on its impact on TGF-β signaling and cell migration. It also evaluates the potential of combining trastuzumab with the integrin inhibitor cilengitide to overcome resistance associated with ITGB3 levels.

Trastuzumab-resistant HCC1954 and SKBR3 cell lines were generated and analyzed for ITGB3 expression heterogeneity. The impact of ITGB3 on TGF-β responsive genes and cell migration was assessed using luciferase reporter assays, real-time PCR, and migration assays. The effects of combined treatment with trastuzumab and cilengitide were also evaluated.

ITGB3 expression varied significantly among resistant clones, correlating with increased expression of TGF-β responsive genes and enhanced migration markers. Combined treatment with trastuzumab and cilengitide significantly reduced TGF-β signaling and migration-related gene expression, particularly in high ITGB3-expressing cells.

ITGB3 plays a critical role in trastuzumab resistance through modulation of TGF-β signaling, migration, and contributing to tumor heterogeneity. Targeting ITGB3, alone or in combination with cilengitide, offers a promising strategy to resensitize resistant HER2-positive breast cancer cells to trastuzumab. These findings provide valuable insights into the mechanisms of trastuzumab resistance and suggest potential therapeutic avenues for improving patient outcomes.

Keywords: HER2-positive breast cancer, trastuzumab resistance, ITGB3, TGF-β signaling, cilengitide, tumor heterogeneity

Oral Presentation-02

Exploring lipidomic shifts in acute myeloid leukemia cells: The impact of dual inhibition of Mcl-1 and sphingolipid metabolism

Melis Kartal Yandim[1], Mesut Bilgin[2]

[1]Danish Cancer Institute, Lipidomics Core Facility, Copenhagen, Denmark; Izmir University of Economics, Faculty of Medicine, Department of Medical Biology, Izmir, Turkiye

[2]Danish Cancer Institute, Lipidomics Core Facility, Copenhagen, Denmark

Acute myeloid leukemia (AML) is a blood disorder with genetic mutations and varied treatment protocols. Overexpression of the anti-apoptotic molecule Mcl-1 in AML contributes to chemotherapy resistance. Targeting Mcl-1 with the small molecule inhibitor S63845 shows promise, though its mechanism remains unclear. Sphingolipids, essential components of cell membranes, regulate vital processes like proliferation and apoptosis. Disruptions in sphingolipid metabolism in AML can affect chemotherapy responses, with apoptosis possibly mediated through Mcl-1.

This study aimed to investigate the mechanism of S63845 in AML cells and the effects of dual targeting Mcl-1 and sphingolipid metabolism on cell death and lipid profiles using quantitative shotgun lipidomics. IC20 and IC50 values of S63845, Fingolimod, Carmofur, and Opaganib were determined in MV4-11, KG1, and HL60 cell lines. The combination of S63845 and Opaganib showed a synergistic effect, particularly in KG1 and MV4-11 cells. Western blot analysis revealed increased CASP3-c expression and decreased BCL2, BECN1, and STAT3 expression in treated cells. Shotgun lipidomics showed increased ceramide levels and reduced hexosyl, dihexosyl, trihexosyl ceramides, sphingomyelin, and GM3 levels, especially in KG1 cells. Lysophosphatidic acid (LPA), which promotes proliferation and drug resistance, also decreased.

These findings suggest that combining S63845 and Opaganib enhances apoptosis via STAT3 and increases ceramide levels, amplifying the synergistic effect through GM3 and LPA, particularly in KG1 cells.

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Keywords: Acute myeloid leukemia, Mcl-1, bioactive sphingolipids, quantitative shotgun lipidomics

Oral Presentation-03

Exploring the role of epigenetic regulators in Paclitaxel-Resistant NSCLC

Arda Isiklar[1], Buse Cevatemre[2], Hamzah Syed[2], Ceyda Acilan Ayhan[2]

[1]Koc University, Graduate School of Health Sciences, Istanbul, Turkiye

[2]Koc University, Research Center for Translational Medicine, Istanbul, Turkiye; Koc University, School of Medicine, Istanbul, Turkiye

Non- small cell lung cancer (NSCLC), most common type of lung cancer, can be treated with surgery and chemothreapy. On the other hand patients treated by chemothreapy initially benefit from treatment but after some time chemoresistance can occur. In order to discover mechanism behind chemoresistance paclitaxel(pac) resistant NSCLC cells were developped in order to identify a novel path to revert this resistance and uncover mechanisms behind resistance process.

Paclitaxel resistant NSCLC cell lines were developped with dose escalation manner. Initial resistancy was confirmed through SRB and colony formation assay between resistant and parental cells. After resistancy towards pac was confirmed, doubling time properties of the cells were investigated by trypan blue exlusion. Besides that relation of parental and resistant cells to platin agents and other taxanes were evaluated using SRB assay. To uncover the transcriptomic alterations between parental and resistant cells RNA-seq was performed among with epigenetic drug library to target potential epiregulators behind pac resistance.

In summary relative resistance of pac between parental and resistant NSCLC was 40 fold showing an evidence of resistant cells were developped successfully. It was observed that parental cell ploriferate faster compared to resistant compartment. Interestingly there was a slight difference towards other platin and taxane agents. Epigenetic drug library screen reveals that BRPF1 and HDAC inhibitors play a key role in targeting potential epiregulators in resistance reversion towards pac.

In conclusion these findings among with candidate potential epiregulators and transcriptomic alterations could reveal novel agents that can be promising to revert resistance in NSCLC.

Keywords: Taxol, Drug Resistance, Lung, ABCB1

Oral Presentation-04

Comparison of Symptoms with Mutation Results in Patients with FMF Preliminary Diagnosis in the Bolu Region

Ali Osman Arslan[1], Murat Dıramali[2], Murat Alisik[3]

[1]Department of Medical Biology, Bolu Abant Izzet Baysal University, School of Medicine, Bolu, Turkiye
[2]Deparment of Anatomy, Bolu Abant Izzet Baysal University, School of Medicine, Bolu, Turkiye
[3]Department of Medical Biochemistry, Bolu Abant Izzet Baysal University, School of Medicine, Bolu, Turkiye

Aim: Familial Mediterranean Fever (FMF) is an autoinflammatory disease in an autosomal recessive manner. Phenotypic effects may vary according to genetic background. It was aimed to investigate the relationship between genotype and symptoms in order to diagnose this disease, which is common in Bolu region. We aimed to compare R202Q, E148Q, M680I, M694V, M694I, V726A, A744S and F479L mutations with disease symptoms in patients with FMF pre-diagnosis.

Method: The sample group consisted of 250 individuals referred or directly applied to Department of Medical Genetics of İzzet Baysal Education and Research Hospital diagnosed with FMF. Mutations were studied with RT PCR. In our retrospective study, data were obtained by scanning patient results.

Result: In our results, the age of onset, joint pain, fever and skin rash findings were found to be associated with gender (p=0.002, p=0.001, p=0.026). Age of onset was found to be significant in abdominal pain complaints (p=0.026). R202Q was found to be associated with abdominal pain, joint pain and chest pain (p=0.056, p=0.042, p=0.02). M694V was found to be significant for skin rash (p=0.043). F479L was found to be associated with abdominal pain (p=0.01).

Conclusion: Our results were generally consistent with the literature. It was observed that R202Q and E148Q mutations were more frequent in Bolu and were statistically significant compared with the symptoms of the disease. So the identification of mutant genes shed light on the pathogenesis of the disease and determines which symptoms are more common in which mutations will support diagnosis and treatment

Keywords: FMF, R202Q, E148Q, M694V, PCR, Abdominal pain

Oral Presentation-05

Effects of PGR gene expression and H770H (rs1042839) mutation on tumor and clinical characteristics in glioma

Ozlem Kurnaz Gomleksiz[1], Merve Nur Aksakal[1], Adil Meric Altınoz[2], Mahmut Ozden[3], Melih Bozkurt[3]

[1]Department of Medical Biology, School of Medicine, Altınbaş University, Istanbul, Turkiye
[2]Department of Medical Biochemistry, Acıbadem University, Istanbul, Turkiye
[3]Depatment of Neurosurgery, Memorial Bahcelievler Hospital,Istanbul, Turkiye

Progesterone, a neurosteroid produced in neurons and glial cells, affects neuronal excitability, learning, and neoplastic proliferation of glial cells. Progesterone binds to the nuclear receptor in its target cells and acts as a transcription factor. The studies on progesterone receptor (PGR) expression and gliomas are controversial. Therefore, it is important to clarify the mutations in PGR gene and the relationships of other factors that may affect the transcription of PGR in elucidating the pathogenesis of gliomas. We aimed to determine the effects of PGR H770H silent mutation, which has not been investigated in detail in glioma, on PGR expression and the relationship of PGR expression with glioma characteristics.

PGR gene expressions were analyzed using qPCR, and H770H was detected by allelic-discrimination assay in 89glioma and 12peripheral tumor tissues. H770H was also analysed in the 44 healthy volunteers, as a control.

High-grade glioma with AA-genotype was more common in males than females (89.2%vs.17.1%, p=0.031). In high-grades, the A-allele frequency is lower in p53-mutation than in p53-wild type (28.6%vs.71.4%, p=0.047). P53 immunoreactivity is also lower in the A-allele than in GG (33.72%vs.99.0%, p<0.001). P53 immunoreactivity was lower in women with high-grade and A-allele than in those with GG (39.86%vs. 99.00%,p=0.003). PGR expression is higher in low-grade gliomas than in high-grades(p>0.05). In the low-grade, the G-allele was associated with lower PGR expression(p=0.026).

Our preliminary findings showing that low-grade gliomas have higher PGR expression point to the association of the PGR with gliomas. Most importantly, H770H mutation can be evaluated as a prognostic marker for gliomas through its effects on p53 status and PGR expression.

Keywords: Progesterone receptor, gene expression, Glioma, H770H

Oral Presentation-06

Evaluation of Nrf2 Gene and Keap 1 Enzyme Levels in Bladder Cancer

Mehmet Aydın Dagdeviren[1] , Mehmet Ozaslan[1], Sibel Bayil[2], Omer Eronat[3]

University of Gaziantep Department of Biology[1], Vocational School of Health, University of Gaziantep[2], University of Gaziantep Faculty of Medicine Pathology Department[3]

Backgraund/Aim: Bladder cancer is the most common type of cancer worldwide. Recent studies have focused on genes that control cell proliferation in the fight against cancer, and the important effects of the Nrf2 gene on cancer have been revealed. Nrf2 is the master regulator of cytoprotective gene. It plays an important role in the regulation of genes involved in cell proliferation, such as P53 and P27, and is induced by the Keap1 enzyme in the cytoplasm by binding to its active site. Therefore, in this study, we compared the quantitative levels of the Nrf gene and Keap1 enzyme in the bladder tissues of patients with low- and high-grade bladder cancer.

Material/ Method: Our research was conducted by taking samples from the bladder tissues of a total of 96 patients with 48 low-grade and 48 high-grade bladder cancer. Tissue samples were analyzed by ELISA method after homogenization and the obtained data were evaluated statistically.

Results: According to the results of the study, the Nrf2 gene was found to be increased while the Keap1 enzyme was decreased in patients with low-level bladder cancer. This shows that cell proliferation in low-level patients is controlled by this mechanism. On the other hand, in patients with high-grade bladder cancer, the Keap1 enzyme was increased and the Nrf2 gene remained at low levels.

Conclusion: These findings suggested that the effectiveness of this regulatory mechanism was lost in patients with high levels and the Nrf2 gene was not sufficiently induced by the Keap1 enzyme.

Keywords: Nrf 2, Keap 1 Enzyme, Bladder Cancer, P53, P27

Oral Presentation-07

Effects of PPAR-gamma Agonists on in-vitro Diabetic Models of Oestrogen-Positive Breast Cancer

Melike Sag[1], Hulya Yilmaz Aydogan[2], Oguz Ozturk[2]

[1]Department of Molecular Medicine, Istanbul University, Istanbul, Turkiye; Department of Molecular Biology and Genetics, Demiroğlu Bilim University, Istanbul, Turkiye
[2]Department of Molecular Medicine, Istanbul University, Istanbul, Turkiye

Breast cancer and Type 2 Diabetes Mellitus (T2DM) are the leading causes of morbidity and mortality worldwide. Research shows that T2DM plays a role in breast carcinogenesis with decreased survival.

Despite strong cytotoxicity, many chemotherapeutics cause severe side effects in breast cancer patients. Searched for safer chemopreventives and chemotherapeutics, some natural polyphenols with few side effects were shown to have preclinical anticancer activities.

Known for their impacts on lipid/carbohydrate metabolism, Peroxisome Proliferator-Activated Receptor-gamma (PPAR-gamma) agonists have effects for and against breast carcinogenesis depending upon cell conditions and stimulation of proliferative and apoptotic signals. PPAR-gamma isoforms function in pathways shared by T2DM and breast cancer. These receptors are among the molecular targets against T2DM and thought to be targeted in breast cancer.

Since PPAR-gamma is involved in common pathways of these two diseases, individual and synergistic effects of its synthetic and natural ligands were investigated upon non-diabetic and diabetic oestrogen-positive breast cancer MCF-7 cell lines modeled by incubation in physiological and supraphysiological glucose and insulin environments. To that end, antidiabetic agent and PPAR-gamma activator Metformin Hydrochloride (MetHCl), Polyphenolic Cocktail (PFK5120) composed of miscellaneous natural polyphenols, and MetHCl-PFK5120 combination (MIKS) were administered on the cells grown under low-glucose (LG), controlled (DC+) and uncontrolled (DC-) hyperglycemic/hyperinsulinemic conditions. Finally, MIKS was observed to be more cytotoxic on the MCF-7_LG cell line, MetHCl in MCF-7_DC+, and PFK5120 in MCF-7_DC- cells.

This study holds promise to develop novel combination therapies and support to conventional therapies for patients with concurrent T2DM and oestrogen-positive breast cancer.

Keywords: breast cancer, T2DM, PPAR-gamma, metformin, polyphenol, MCF-7

Oral Presentation-08

Ylang ylang oil might induce mitophagy in lung cancer cell lines

Baris Ertugrul[1], Göksu Kasarcı Kavsara[1], Tugba Buse Şentürk[3], Timur Hakan Barak[3], Sinem Bireller[2], Bedia Cakmakoglu[1]

[1]Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkiye
[2]Department of Biochemistry, Faculty of Pharmacy, Acibadem Mehmet Ali Aydinlar University, Istanbul, Turkiye
[3]Department of Pharmacognosy, Faculty of Pharmacy, Acibadem Mehmet Ali Aydinlar University, Istanbul, Turkiye

Natural anticancer molecules are promising therapeutic alternatives due to their low toxicity and ability to target cancer cells. Lung cancer is the most common type, accounting for 11.6% of all cases and leading in global cancer deaths [1,2]. This study aimed to investigate the effects of Ylang Ylang essential oil (YYE), known for its rich sesquiterpene content, on lung cancer and its relationship with the mitophagy pathway [3,4].

Phytochemical evaluation of YYE was performed using GC-MS analysis, identifying major metabolites (Figure 1). The study assessed YYE's cytotoxicity on various respiratory-related cell lines (Table 1), as well as its effects on cell membrane integrity, total antioxidant capacity, and mitophagy-related gene expression using CCK-8, LDH assays, and RT-PCR (Table 2). YYE at 1250 µg/mL and 1500 µg/mL on A549 cells resulted in 24.89% and 54.43% LDH activity, while healthy cells showed no toxicity ($p<0.05$). YYE also exhibited greater antioxidant activity than the reference antioxidant, Trolox.

Preliminary findings suggest that YYE interacts with lung cancer cells through various pathways, showing no harmful effects on healthy cells. YYE demonstrated effects on mitophagy, particularly through the receptor-mediated mitophagy pathway (BNIP3/NIX) in lung cells. Given the role of mitochondria in ROS production and the importance of mitochondrial quality control in health and disease, YYE's activity on mitochondrial mechanisms highlights its potential as a promising agent and treatment option for lung cancer.

Keywords: Cananga odorata, Ylang Ylang, mitophagy, cancer

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Oral Presentation-09

Hedgehog Pathway is a Regulator of Stemness in Her2-Positive Trastuzumab Resistant Breast Cancer

Idris Er[1], Asiye Busra Boz Er[2]

[1]Department of Medical Biology, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkiye
[2]Department of Medical Biology, Faculty of Medicine, Recep Tayyip Erdogan University, Rize, Turkiye

HER2 overexpression is observed in 20-30% of breast cancers and is associated with a poor prognosis. Trastuzumab, a monoclonal antibody targeting HER2, is a standard therapy for HER2-positive breast cancer. However, resistance develops in approximately 50% of patients within a year, necessitating new therapeutic strategies. The Hedgehog (Hh) signaling pathway, known for maintaining cancer stem cell properties (stemness), may contribute to trastuzumab resistance in HER2-positive breast cancer.

This study investigated the role of Hedgehog signaling in sustaining stemness and promoting trastuzumab resistance in HER2-positive breast cancer cell lines. Trastuzumab-resistant SKBR3 and HCC1954 cell lines were generated through continuous trastuzumab exposure. Cells were treated with GANT61 (Hh inhibitor, 10 μM) or SAG21K (Hh activator, 100 nM) for 24 hours to evaluate the response of Hedgehog signaling. Stemness marker expression (Nanog, Sox2, Bmi1, Oct4) was measured using qRT-PCR. The combination index (CI) for GANT61 with trastuzumab was calculated using CompuSyn software to determine synergistic doses (CI < 1). The effects of these doses on stemness markers were assessed. Data were analyzed using two-way ANOVA and Tukey's post hoc test ($p < 0.05$).

Trastuzumab-resistant cells showed upregulated Hedgehog signaling. GANT61 reduced, while SAG21K increased stemness marker expression in both resistant cell lines. The combination of GANT61 with trastuzumab had a synergistic effect, significantly lowering stemness markers. These findings suggest that Hedgehog signaling supports stemness in resistant cells and that targeting this pathway could enhance trastuzumab efficacy. Further research should explore the clinical potential of Hedgehog inhibitors in combination therapies.

Keywords: Stemness, Trastuzumab Resistant, Her2-Positive Breast Cancer, Hedgehog Pathway

Oral Presentation-10

Determining the association between GDF-15 gene variants and Type 2 Diabetes: A hospital-based case-control study

Emine Yagci[1], Gamze Zengin[1], Cansu Ozbayer[1], Melike Bayindir Ureten[1], Medine Nur Kebapci[2], Irfan Degirmenci[3], Hulyam Kurt[3]

[1]Kutahya Health Sciences University, Medical Faculty, Department of Medical Biology, Kutahya, Turkiye
[2]Eskisehir Osmangazi University, Medical Faculty, Department of Endocrinology, Eskisehir, Turkiye
[3]Eskisehir Osmangazi University, Medical Faculty, Department of Medical Biology, Eskisehir, Turkiye

Type 2 Diabetes Mellitus (T2DM) is one of the most common metabolic disorders worldwide and its development is mainly caused by defective insulin secretion by pancreatic β-cells and the failure of insulin-sensitive tissues to respond to insulin.

Growth differentiation factor-15 (GDF-15) is a member of the transforming growth factor-beta (TGF-β) superfamily that plays multiple roles in various cellular processes. GDF-15 is widely expressed in liver, skeletal muscle, kidney, heart or macrophage, is a direct molecular target of p53 protein and is considered a marker of inflammation and oxidative stress induced by tissue damage, hypoxia and proinflammatory cytokine response. Studies have shown that GDF-15 expression levels can be significantly increased in response to various physiological conditions associated with obesity, insulin resistance, tissue damage, inflammation, diabetes and various malignancies. Our study aimed to determine the association between GDF-15 rs4808793 and rs1058587 variants and the risk of T2DM. Seventy healthy controls and seventy endometrial T2DM patients participated in this case-control research. Blood samples were used to obtain genomic DNA, and the PCR-RFLP method was used to determine genotypes.

GDF-15 rs4808793 and rs1058587 genotype distributions were found to differ significantly between the T2DM and control groups ($p<0.05$). In addition, while GDF-15 rs1058587 allele frequencies were found to be significantly different between the T2DM and control groups, no significant difference was found in terms of GDF-15 rs4808793 allele frequencies.

As a conclusion, the GDF-15 rs4808793 and rs1058587 variations were determined to be closely associated with T2DM risk.

Keywords: Type II Diabetes, GDF-15, inflammation, biomarker

Oral Presentation-11

Testing of 1.7A2UCOE, 1.2A2UCOE and O.5UCOE Universal Chromatin Opening Elements (UCOE) Derived from Hnrpa2b1-Cbx3 Reference Gene Loci on Human Stem Cells (iPS Cells)

Omer Faruk Anakok[1], Livanur Yücel, Hassana Adamou Ali

[1]Bolu Abant İzzet Baysal University, Faculty of Medicine, Molecular Genetics

This project aims to provide a universal solution to the problems of low-level binding and inactivation in mammalian cells, such as gene silencing, histone modifications and vector-driven transfection applications, which are frequently encountered in in-vivo and in-vitro gene therapy, genetic modifications and recombinant protein biotechnology studies.The aim of this project is to test the universal chromatin opening potentials of the new generation 1.7A2UCOE and 1.2A2UCOE ubiquitous chromatin opening element models against the methylation and histone modification problems frequently encountered in gene therapy studies on human stem cells and after differentiation into three different tissue types.

Our results showed that the new UCOE designs (1.2kb and 1.7kb UCOE chromatin elements) that we developed, have maintained their expression levels stably on human iPS cells before and after differentiation into three different tissue type cells. In addition, our new 0.5kb design (0.5kb UCOE), produced from another CpG density region of HNRPA2B1 gene, which has not been studied before in the literature, has been observed to display a stable expression level compared to our other designs and even a more stable profile. This result is beyond the target in our project, with the length of 5kb-3kb (without supporting, expression-enhancing cassette regions) and 1.5kb (with supporting, expression-enhancing cassette regions), the new 0.5kb, 1.2kb 1.7kb (without supporting, expression enhancing cassette regions, thus eliminating the potential mutation problem) with a length of 10, 6 and 3 times shorter than the current standard A2UCOE models showed to be more advantageous for gene therapy and recombinant protein production studies.

Keywords: Gene Therapy, Lentiviral vectors, Chromatine Opening, UCOE

Oral Presentation-12

Effects of the VDR rs757343 (T>A) polymorphism in MODY patients

Sura Edanur Saglam[1], Beyzanur Simsek Cetin[1], Aref Khalkhali[1], Bita Rostami[1], Ilhan Satman[2], Nurdan Gul[2], Ozlem Kurnaz Gomleksiz[3], Hulya Yilmaz Aydogan[4], Deniz Kanca Demirci[1]

[1]Department of Molecular Biology and Genetics, Faculty of Arts and Sciences, Haliç University, İstanbul, Turkiye.
[2]Department of Internal Medicine, Division of Endocrinology and Metabolism, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkiye.
[3]Department of Medical Biology, Faculty of Medicine, Altınbaş University, Istanbul, Turkiye.
[4]Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkiye.

Objectives: Vitamin D levels is associated with insulin resistance and contributes pathogenesis of diabetes. VD functions with its receptor (VDR) and VDR mutations play a role in development of diabetes. We aimed to investigate the effects of VDR-rs757343 SNP on metabolic and clinical features in patients with clinically-diagnosed maturity-onset-diabetes-of-the-young (MODY).

Materials-Methods: VDR-rs757343 polymorphism is analyzed by PCR-RFLP in 63 patients with MODY and 61 healthy-control subjects. Statistical analyses were performed by SPSS v.24.0.

Results: In the MODY patient group weight ($p=0.021$), BMI ($p<0.001$), WC ($p<0.001$), HC ($p<0.001$), FBG ($p<0.001$), HbA1c ($p<0.001$), TG ($p=0.007$), GGT ($p=0.001$), hs-CRP ($p<0.001$) and fT4 ($p=0.039$) values were found higher and statistically significant, while HDL-C ($p=0,043$) value was found lower compared to the healthy control group.

It was observed that TG levels were higher ($p=0.008$) and TSH levels were lower ($p=0.042$) in the patients with GG genotype compared with A-allele and in the control group, higher BMI ($p=0.051$) and hip-circumference ($p=0.050$) levels were seen the GG genotype carriers in those carrying A-allele (Table 3).

Higher TG levels ($p=0.045$) and lower TSH levels ($p=0.042$) were observed in the patients with GG genotype compared to GA genotype while lower SBP ($p=0.030$) and higher TSH ($p=0.057$) levels in those carrying GG genotype compared to the healthy-subject with GA genotype with ANOVA analysis (Table 4).

Conclusions: Our findings show that the VDR-rs757343 (T>A) mutant GG genotype was effective on parameters related to lipid and thyroid metabolism. Therefore, further studies with larger sample sizes are required for stronger findings.

Keywords: MODY, VDR, rs757343, SNP, TG, TSH

Oral Presentation-13

Effects of oxidative stress caused by methotrexate and aging on reproductive hormones

Sukriye Caliskan[1], Sehkar Oktay[2]

[1]Health Sciences Institute, Department of Biochemistry, Faculty of Pharmacy, Marmara University, Istanbul, Turkiye
[2]Department of Basic Medical Science, Biochemistry, Faculty of Dentistry, Marmara University, Istanbul, Turkiye

Objective: Several established risk factors for many diseases have been linked to oxidative stress. Methotrexate (MTX) is a cytotoxic drug used in cancer treatment via chemotherapy. Just as MTX has side effects on many organs, the reproductive system has also been affected by MTX administration. Aging is a natural factor comprising changes in the systems and organs. The study aimed to investigate the effect of oxidative stress resulting from methotrexate administration and aging on Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH), and testosterone hormones in sera of young and adult male rats.

Materials-Methods: Twenty-four Wistar Albino rats were divided equally into 4 groups: Young controls (YC) (2-month-old rats), adult controls (AC) (9-month-old rats), MTX-given young group (YMT) (MTX given 2-month-old rats), and MTX-given adult group (AMT) (MTX given 9-month-old rats). MTX was injected with a single dose of 20 mg/kg, i.p. Sera samples were taken to analyze LH, FSH and testosterone hormones of the rats.

Results: MTX administration significantly decreased LH, FSH, and testosterone levels in the AMT group compared to the YC and YMT groups. There was a slight decrease in hormone levels of the AC groups compared to the YC group, but the results were insignificant.

Conclusion: MTX treatment can trigger radical formation in the body and cause potential reproductive health problems, especially in adults. Besides, it may become more difficult to avoid the side effects of MTX with age.

Keywords: Methotrexate, Luteinizing Hormone, Follicle-Stimulating Hormone, Testosterone, Oxidative Stress

Oral Presentation-14

Investigation of the Effects of Doxorubicin on MTR, BCAT1 and PHGDH Genes in Mcf-7 Cell Line

Arda Kebapci[1], Levent Gulum[5], Kezban Ucar Cifci[3], Merve Nur Al[2], Yusuf Tutar[4]

[1]İstanbul Medipol University, Research Institute for Health Sciences and Technologies (SABITA)
[2]Sağlık Bilimleri Üniversitesi
[3]Division of Basic Sciences and Health, Hemp Research Institute, Yozgat Bozok University, Yozgat, Turkiye
[4]Recep Tayyip Erdoğan Üniversitesi
[5]Bolu Abant İzzet Baysal Üniversitesi

Aim: Breast cancer is one of the most commonly diagnosed diseases among women worldwide and represents a significant cause of mortality. Doxorubicin (DOX), a topoisomerase II inhibitor that induces apoptosis via oxidative DNA damage, is commonly used in its treatment. This study aims to identify novel molecules involved in metabolic pathways contributing to doxorubicin resistance.

Materials-Methods: Doxorubicin-sensitive (MCF-7) and -resistant (MCF-7/ADR) breast cancer cell lines were utilized. The IC50 values of doxorubicin in MCF-7 cells were determined by MTT assay. Gene expression of MTR, BCAT1, and PHGDH involved in amino acid metabolism was analyzed in both cell lines using RT-qPCR.

Results: The IC50 value of doxorubicin in MCF-7 cells was 0.0027 µM ($p<0.001$). The same concentration was applied to MCF-7/ADR cells. Comparative analysis using the 2 -ΔΔCt method revealed significant decreases in the expression of all three genes in MCF-7 cells. In contrast, no significant changes were observed in the expression of MTR and PHGDH genes in MCF-7/ADR cells, although a partial decrease in BCAT1 expression was detected.

Conclusion: Resistance to doxorubicin in MCF-7/ADR cells leads to alterations in the expression levels of genes related to amino acid metabolism. These findings may contribute to a more detailed evaluation of potential therapeutic strategies in breast cancer treatment.

Keywords: Breast Cancer, Doxorubicin, MCF-7, Metabolism

Oral Presentation-15

New and Effective Compounds for Alzheimer's Disease and Cancer Therapy: Design, Synthesis and Biological Evaluation Studies

Kadircan Ural[1], Ferah Comert Onder[2]

[1]Department of Medical System Biology, School of Graduate Studies, Çanakkale Onsekiz Mart University, 17020, Çanakkale, Turkiye
[2]Department of Medical Biology, Faculty of Medicine, Çanakkale Onsekiz Mart University, 17020, Çanakkale, Turkiye

Alzheimer's disease (AD) is a complex neurodegenerative disorder which characterized by progressive cognitive decline and memory loss. Pathological feature of AD is the decreased levels of acetylcholine (ACh) due to the hyperactivity of cholinesterases, such as acetylcholinesterase (AChE). For this purpose, new and effective AChE inhibitors is crucial as existing treatments often have limitations in efficacy and side effects. Benzopyran ring containing compounds have garnered significant attention due to their diverse biological activities, particularly in the context of AD and cancer treatment. Therefore, this study aimed to design of new candidates targeting AChE for AD using in silico methods and evaluate their in vitro enzyme-activity and anticancer potentials. These synthesized compounds were characterized by using FTIR, 1H-NMR,13C-NMR, and LC-MS/MS spectroscopic analysis.

Molecular docking and molecular dynamics (MD) simulations demonstrated that these candidates exhibited strong binding affinity to AChE with key interactions in the binding pocket of target enzyme compared to known inhibitors Donepezil, Tacrine, and Rivastigmine. These compounds were interacted with the critical amino acids of AChE. In silico ADMET predictions confirmed that the favorable druglikeness properties of the compounds. According to our in vitro enzyme-activity results, the synthesized compounds were showed strong inhibitor effects with IC50 values in the range of 20-100 nM for AChE inhibition compare to known inhibitors. Additionally, cell proliferation assays showed that some of the synthesized compounds were exhibited strong activity in various cancer cell lines.

Overall, our findings suggest that these synthesized compounds will be promising candidates for AD treatment and cancer therapy.

Keywords: Alzheimer's disease, Cancer, synthesis, inhibitor, enzyme inhibition, in silico

Acknowledgement: This study was supported by the Çanakkale Onsekiz Mart University Research Coordination Unit (Project No: TYL-2024-4744).

Oral Presentation-16

In Silico, Synthesis, In Vitro Enzyme-Activity of New and Potential Inhibitor Candidates for Alzheimer's Treatment and Their Antiproliferative Effects

Merve Sıkık[1], Ferah Comert Onder[2]

[1]Department of Medical System Biology, School of Graduate Studies, Çanakkale Onsekiz Mart University, 17020, Çanakkale, Turkiye
[2]Department of Medical Biology, Faculty of Medicine, Çanakkale Onsekiz Mart University, 17020, Çanakkale, Turkiye

Alzheimer's disease (AD) is a severe neurodegenerative disorder characterized by cognitive impairments and memory loss, which is increasingly prevalent among the aging population. Due to the limited efficacy of current treatment options, there is need to develop new and more effective therapeutic agents for AD treatment. Therefore, in this study, new compounds as potential acetylcholinesterase (AChE) inhibitor candidates were designed and synthesized, and investigated in silico analysis including virtual screening, molecular docking, and molecular dynamics (MD) simulations. These synthesized compounds were characterized by using FT-IR, 1H and 13C NMR, and LC-MS/MS spectroscopic methods. In silico pharmacokinetic and toxicological profiles of these synthesized novel inhibitor candidates were predicted by ADMET analysis. The inhibitory activities of the synthesized compounds against AChE were detected by using the Ellman Method in in vitro studies. Furthermore, the synthesized compounds exhibited significant antiproliferative effects on triple-negative breast cancer (TNBC) and colon cancer cell lines. In silico results show that the newly designed and synthesized compounds bind to AChE with high binding affinity compared to known inhibitors Donepezil, Tacrine, and Rivastigmine. We obtained strong inhibitory effects with these compounds in in vitro enzyme activity assay. The tested compounds had IC50 values for AChE inhibition in the ranging values. In addition, the synthesized compounds exhibited strong antiproliferative effects on various cancer cell lines.

Overall, our findings suggest that these compounds could serve as promising candidates for AD treatment and cancer. This study may present new approaches for developing new inhibitors for AD and cancer treatment.

Keywords: Alzheimer's disease, Cancer, Synthesis, Inhibitor, Enzyme Inhibition, In silico

Acknowledgement: This study was supported by the Çanakkale Onsekiz Mart University Research Coordination Unit (Project No: TYL-2024-4743).

Oral Presentation-17

Development and Clinical Validation of an Oxford Nanopore-Based Multigene Panel for the Diagnosis of Carnitine Cycle Defects

Gokce Akan[1], Mehmet Cihan Balci[2], Gülten Tuncel[1], Meryem Karaca[2], Hasan Hüseyin Kazan[3], Ahmet Caglar Ozketen[1], Ozge Ozgen[4], Asuman Gedikbasi[5], Gulden Fatma Gokcay[6], Fatmahan Atalar[6]

[1]DESAM Institute, Near East University, Mersin, Turkiye
[2]Division of Pediatric Nutrition and Metabolism, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkiye
[3]Department of Medical Biology, Gulhane Faculty of Medicine, University of Health Sciences, Ankara, Turkiye
[4]Rare Diseases Research Laboratory, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkiye
[5]Department of Pediatric Basic Sciences, Child Health Institute, Istanbul University, Istanbul, Turkiye
[6]Department of Rare Diseases, Child Health Institute, Istanbul University, Istanbul, Turkiye

Background: Carnitine cycle defects (CCDs) are newborn metabolic disorders characterized by reduced carnitine levels, leading to symptoms ranging from mild fatigue to severe cardiac complications. Prompt diagnosis and treatment are essential to prevent morbidity and mortality. However, CCD diagnosis is challenging due to its heterogeneous presentation and limited genetic tests. Oxford Nanopore Technologies (ONT) offers cost, labor, and time efficiencies in genetic testing. This study aimed to develop and clinically validate an ONT-based multigene panel for CCD diagnosis.

Materials-Methods: A multiplex PCR-based panel was developed to generate 4–7 kb amplicons covering the CPT1A, CPT2, SLC25A20, and SLC22A5 genes. Twenty-one primer pairs were designed for analysis using the ONT MinION system. The panel was optimized with reference DNA and validated with samples from 18 patients with confirmed CCD diagnoses from second-generation sequencing platforms.

Results: Two primer pools successfully covered all pathogenic and likely pathogenic variants, including exonic and intronic regions of CCD-related genes. The expected base coverage of 200X read depth was achieved for all samples within 7 hours. A 100% concordance was observed between ONT and second-generation platforms in detecting pathogenic/likely pathogenic variants. Common mutations identified included CPT1A: c.740C>T (p.Pro247Leu), CPT2: c.338C>T (p.Ser113Leu), and SLC22A5: c.454G>C (p.Gly152Arg).

Conclusion: This study introduces the first ONT-based multigene panel for CCD diagnosis Using multiplex PCR-based target enrichment with ONT sequencing provides an efficient approach for analyzing CCD-responsible genes.This method can potentially facilitate rapid, cost-effective diagnosis and management as the second-tier testing platform with enhanced sensitivity and multiplex gene analysis for early detection.

Keywords: Carnitine cycle defects, Newborn screening, Diagnosis, DNA Sequencing, Oxford Nanopore sequencing technology

Oral Presentation-18

Investigation of Umami Taste TR1/TR3 Receptor Expression Levels in Rat Peripheral Tissues in the NMDAR Hypofunction Model

Duygu Vardaglı[1], Karolin Yanar[2], Zeliha Emel Zengin[3]

[1]Istanbul Esenyurt University, Health Services Vocational School, Medical Laboratory Techniques Program,İstanbul,Turkiye
[2]Istanbul University-Cerrahpaşa, Faculty of Medicine, Department of Medical Biochemistry,İstanbul, Turkiye
[3]Baskent University, Baskent University Istanbul Hospital,Department of Medical Biochemistry,Istanbul,Turkiye

In the NMDAR hypofunction model, investigation of other receptors compatible with the NMDA receptor and peripheral tissues that may be a reference to the brain tissue is essential for the detection of the disease in the prodramal stage. For this reason, in the modeling performed with NMDAR hypofunction, TR1/TR3 receptor expression levels, whose common substrate is L-glutamate and provides umami taste perception, were measured and it was investigated whether free radical formation had an effect on hypofunction.

ELISA method was used to determine the expression levels of NMDAR and TR1/TR3 in all groups. Copper-zinc superoxide dismutase activity was studied spectrophotometrically according to Sun's method. Advanced oxidation protein products were analyzed spectrophotometrically according to the method of Hanasand. To determine the level of oxidation, the amounts of dityrosine, advanced glycolization products and kynurenine were also measured using fluorometric methods. For the statistical evaluation of the experimental results in our study, Indepent sample t test will be applied to the groups and $p < 0.05$ will be considered significant.

TR1 and TR3 expression levels responded to modeling only in the kidney tissue and in an increasing direction. Oxidation parameters in the modeling, maintained control levels in the kidney tissue.

Only kidney tissue responded to NMDAR hypofunction in the periphery by increasing TR1 and TR3 expression levels. The fact that oxidative damage developing in other tissues was not detected in the kidney suggests that this increase is a response to hypofunction rather than a compensation mechanism.

Keywords: NMDAR, Umami Taste, TR1/TR3, Schizophrenia, Taste Receptors

Oral Presentation-19

Effects of Nanoplastics on Locomotor and Acetylcholinesterase Activities of Developing Zebrafish Embryos

Zulal Mizrak[1], Semanur Isikoglu[1], Merih Beler[1], Gizem Egilmezer[1], Ismail Unal[2], Derya Cansiz[2], Ebru Emekli Alturfan[3]

[1]Marmara University, Institute of Health Sciences, Department of Biochemistry, Turkiye
[2]Istanbul Medipol University, Faculty of Medicine, Department of Biochemistry, Turkiye
[3]Marmara University, Faculty of Dentistry, Department of Basic Medical Sciences, Turkiye

Microplastic pollution has gained significant attention over the past decade due to its environmental and health impacts. Microplastics (MP), defined as particles ranging from 100 nanometers to 5 millimeters, and those with diameters smaller than 100 nanometers are referred to as nanoplastics (NP). They are widespread in aquatic environments due to their small sizes. The presence of MP and NP in the sea represents a significant environmental hazard, as well as a threat to the aquatic organisms with studies showing that they can accumulate in organisms, cross biological barriers, and cause adverse effects such as oxidative stress, neurotoxicity, and inflammation. The zebrafish is a suitable model organism for the study of various organ systems and biological pathways.

The aim of this study was to evaluate the neurotoxic effects of the NP exposure on developing zebrafish embryos. Zebrafish embryos were exposed to 100 nm NP (Magsphere) at different concentrations for up to 120 hours post fertilization (hpf). Developmental parameters, mortality rates, hatching rates, locomotor activity, and acetylcholinesterase activity were analyzed.

Significant alterations were observed in the parameters of the NP exposed embryos when compared with the control group. Delayed hatching, developmental defects, and increased mortality rates were observed in the zebrafish embryos exposed to the highest concentration of NP (1000 µg/l) compared to the control group and the lower concentrations.

When all these results are evaluated, NPs showed toxic effects on the locomotor and cognitive development of zebrafish embryos. These results have emphasized the importance of MP/NP pollution in the sea.

Keywords: Nanoplastics, development, neurotoxicity, zebrafish embryos

Oral Presentation-20

A First Preliminary Report: Potential Implications of IDO1 Expression on Soluble Tryptophan and Tryptophan Catabolites in Gastric Tumors and Tumor Microenvironment

Cem Horozoglu[1], Mehmet Tolgahan Hakan[2], Safak Sener[3], Dilara Sonmez Zor[2], Fikret Aktas[4], Ozlem Kucukhuseyin[2], Soykan Arikan[5], Filiz Akyuz[6], Ilhan Yaylim[2]

[1]Halic University, Faculty of Medicine, Department of Medical Biochemistry, Istanbul, Turkiye
[2]Istanbul University, Aziz Sancar Institute of Experimental Medicine, Department of Molecular Medicine, Istanbul, Turkiye
[3]Halic University, Faculty of Arts and Sciences, Department of Molecular Biology and Genetics, Istanbul, Turkiye
[4]Charité – Universitätsmedizin Berlin, Germany
[5]Basaksehir Cam and Sakura City Hospital, Department of General Surgery, Istanbul, Turkiye
[6]Istanbul University, Faculty of Medicine, Gastroenterology, Istanbul, Turkiye

Aim: Indoleamine 2,3-Dioxygenase 1 (IDO1)-mediated tryptophan degradation products are associated with the process of carcinogenesis in different cancers. IDO1, whose overexpression at the tumor site causes low survival, metastasis and differentiation, also affects the functions of immune system cells in the tumor microenvironment, leading to suppression of the immune system and thus to the development of tumor-related mechanisms such as metastasis and angiogenesis. In our study we aim In this study, we aim to investigate the relationship between IDO1 and tryptophan/kynurenine pathway in gastric cancer tumor tissue and microenvironment.

Method: IDO1 expression was analyzed using quantitative PCR (q-PCR) method in 102 gastric cancer (GC) samples, both tumor tissue and the surrounding microenvironment. Serum levels of tryptophan, kynurenine, and kynurenic acid were measured via High Pressure Liquid Chromatography-Fluorescence Detector (HPLC-FD) in 51 GC patients and 49 healthy controls.

Result: IDO1 expression was observed 3.25 times lower compared to the tumor microenvironment ($p=0.05$) in gastric tumors. In GC, tryptophan levels were identified approximately 1.6 times higher at a significant level (AUC: 0.889; cut-off <=21.57; $p<0.001$).

Discussion: When metabolized through the IDO1 pathway, increased tryptophan accumulation in the gastric tumor and its microenvironment plays a significant role.

Acknowledgments: This study was funded by Scientific Research Projects Coordination Unit of Istanbul University. Project number TYO-2019-33675

Keywords: Gastric cancer, Indoleamine 2, 3-Dioxygenase 1, Tryptophan, Kynurenine

Oral Presentation-21

Investigation of Co-expression of lncRNA SNHG1 and miR-153-3p in Tumor and Tumor Microenvironment of Gastric Cancer Cases

Safak Sener[1], Cem Horozoglu[2], Hazal Karadag[3], Asli Yildiz[3], Mehmet Tolgahan Hakan[4], Soykan Arikan[5], Ilhan Yaylim[4]

[1]Halic University, Faculty of Arts and Sciences, Department of Molecular Biology and Genetics, Istanbul, Turkiye
[2]Halic University, Faculty of Medicine Department of Medical Biochemistry, Istanbul, Turkiye
[3]Biruni University, Faculty of Medicine, Istanbul, Turkiye
[4]Istanbul University, Aziz Sancar Institute of Experimental Medicine Department of Molecular Medicine, Istanbul, Turkiye
[5]Basaksehir Cam and Sakura City Hospital, Department of General Surgery, Istanbul, Turkiye

Aim: miR-153 has tumor suppressor effects in many solid organ cancers including gastric cancer (GC). Similarly, LncRNA SNHG1 is overexpressed in many solid organ tumors compared to tumor-free surrounding tissues. Our study aims that to decipher the role of mir-153-3p/ lncRNA SNHG1 axis in the pathophysiological direction in gastric cancer.

Method: cDNA synthesis will be performed from total RNA in tumor and tumor-free surrounding tissue of 30 GC patients, and transcript levels of SNHG1 and mIR-153-3p will be determined by RT-PCR. The transcript levels, clinicopathologic parameters of the patients, and demographic information of the patients will be statistically analyzed. Comparison of the levels between tumor and tumor surrounding tissue, the relationship between fold changes and clinicopathological parameters will be evaluated. Pearson or Spearman correlation test will be used to evaluate the co-expression of lncRNA SNHG1 and miR-153.

Result: As a result, relative expression of lncRNA SNHG1 levels was determined as 38.9 (fold change) in tumor tissue and 18.4 (fold change) in tumor-free surrounding tissue compared to GAPDH. A 2.12-fold significant increase was detected in tumor tissue compared to surrounding tissue (p=0.02). Relative expression of miR-153-3p levels was determined as 318.07 (fold change) in the surrounding tissue without tumor and 701.55 (fold change) in tumor tissue. The miR-153-3p level was 2.22 times higher in tumor tissue than in the non-tumorigenic surrounding tissue.

Discussion: The correlation of the SNHG1/mir-153-3p axis in gastric cancer and their higher expression in tumor tissue compared to TMC suggest that this axis has a strong oncogenic effect.

Keywords: Gastric cancer, miR-153-3p, lncRNA, SNHG1

Oral Presentation-22

Investigation of morphological and behavioral alterations in hypoxia-induced zebrafish embryos

Efruz Irem Akkus Yaylamis[1], Derya Cansiz[2], Ismail Unal[2], Merih Beler[3], Mujgan Cengiz[1], Ebru Emekli Alturfan[4]

[1]Istanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Medical Biology, Istanbul, Turkiye
[2]Istanbul Medipol University, Faculty of Medicine, Department of Medical Biochemistry, Istanbul, Turkiye
[3]Marmara University, Institute of Health Sciences, Department of Biochemistry, Istanbul, Turkiye
[4]Marmara University, Faculty of Dentistry, Department of Basic Medical Sciences, Istanbul, Turkiye

Hypoxia, which refers to insufficient oxygen delivery to tissues or organs, is known to affect embryonic development in zebrafish embryos and cause various neurobiological disorders.

This study aimed to investigate morphological and behavioral alterations in zebrafish embryos exposed to hypoxic conditions.

We exposed zebrafish embryos to a controlled hypoxic E3 medium and monitored and documented their embryonic development, mortality, and hatching rates daily up to 72 hours post-fertilisation (hpf) for morphological assessment. Motility analyses were performed to assess locomotor behavior by touch-evoked response method at 72 hpf.

Preliminary results indicate that hypoxia-induced embryos exhibit significant morphological and behavioral aberrations compared to normoxic controls.

These findings suggest that hypoxia may disrupt normal developmental processes, leading to both somatic and behavioral alterations. Our work will continue with investigations aimed at elucidating the molecular mechanisms underlying these changes and contributing to a better understanding of how hypoxic conditions affect embryonic development in the zebrafish model.

Keywords: Hypoxia, development, behavior, locomotor activity, zebrafish embryos

Oral Presentation-23

Comparison of the impact of oleuropein on adult female Drosophila melanogaster fed on sucrose and sucrose+fructose media

Karolin Yanar[1], Sevcan Kutlu[1], Melike Demir[2], Pınar Atukeren[1]

[1]Department of Medical Biochemistry, Cerrahpaşa Faculty of Medicine, Istanbul University-Cerrahpaşa, Istanbul, Turkiye
[2]Cerrahpaşa Faculty of Medicine, Istanbul University-Cerrahpaşa, Istanbul, Turkiye

Drosophila melanogaster is a model organism used for various fields of research such as aging, nutrition, metabolic syndrome and, neurotoxicity. Sucrose is a disaccharide consisting of glucose and fructose. It is commonly used as a standard medium for Drosophila melanogaster. Fructose is a monosaccharide. Its low additive levels may be beneficial for reproduction capacity. On the other hand, high levels may lead to metabolic syndrome due to the high metabolic fate of fructose. Oleuropein is the main phenolic component of Olea europaea L. It has several beneficial features on health and it acts as an antioxidant, anti-inflammatory, and neuroprotective agent depending on its consumption dose and usage duration.

We aimed to evaluate whether oleuropein has any protective effect on adult female Drosophila melonagaster fed on sucrose and sucrose+fructose media. We prepared 4 groups (n=3, with 25 fruity fly/media) as adult female Drosophila fed on sucrose-media, sucrose+fructose-media, sucrose+oleuropein-media (5 mg/L for four hours after 2 hours of starvation period), sucrose+fructose+oleuropein (5 mg/L for four hours after 2 hours of starvation period) media. We analyzed biomarkers of redox homeostasis via spectrophotometric analysis of superoxide dismutase activity (Cu,Zn-SOD) and total thiol (T-SH) content as antioxidant biomarkers and advanced oxidation protein products (AOPP) and spectrofluorometric analysis of dityrosin (DT), kynurenine (KYN) and advanced glycation end products (AGEs) as oxidant biomarkers.

Our analysis showed that oleuropein (5mg/L-4 hours) acts as a pro-oxidant. The preliminary results recommend oleuropein should be consumed carefully and further studies to detect the optimum antioxidant dose are needed.

Keywords: Drosophila melanogaster, sucrose, fructose, oleuropein, redox homeostasis, female

Oral Presentation-24

Investigation of the Effect of Nanoplastic Exposure on The Oxidant-Antioxidant Balance in Zebrafish Embryos

Merih Beler[1], Ismail Ünal[2], Derya Cansiz[2], Gizem Egilmezer[1], Ebru Emekli Alturfan[3]

[1]Marmara University, Institute of Health Sciences, Department of Biochemistry, Turkiye
[2]Istanbul Medipol University, Faculty of Medicine, Department of Biochemistry, Turkiye
[3]Marmara University, Faculty of Dentistry, Department of Basic Medical Sciences, Istanbul, Turkiye

The effects of microplastics on endocrine disruption, neurotoxicity, and the reproductive system have been demonstrated in numerous studies. Additionally, micro and nanoplastics are known to impact lipid, carbohydrate, and protein metabolism. Microplastics/nanoplastics are substances that we are exposed to in many sectors and fields in today's world, where plastic production and consumption are continuously increasing. They are environmental pollutants resulting from the degradation and wear of plastic products. The effects of microplastic (MP) exposure, including oxidative damage, cytotoxicity, neurotoxicity, energy loss, apoptosis mechanisms, and impacts on the reproductive system, have been demonstrated in various model organisms. MPs accumulate in various regions of the body and, by penetrating biological membranes depending on their size, can interfere with biochemical pathways and affect cellular function. The zebrafish (Danio rerio) is one of the important model organisms used in development and toxicology studies. It is known that the accumulation of micro/nanoplastics in the organism over short, medium, and long periods leads to adverse effects on the oxidant-antioxidant balance.

In our study, the effects of 100-nanometer polystyrene particle exposure on growth and development in zebrafish embryos were investigated, with a focus on oxidant-antioxidant parameters. Specifically, superoxide dismutase (SOD), glutathione S-transferase (GST), catalase (CAT), and lipid peroxidation (LPO) activities were analyzed. The morphological effects were also examined to assess developmental changes.

The differences obtained in the oxidant-antioxidant system parameters due to MP exposure showed the toxic effects of MP exposure and revealed the need for new experiments with different doses.

Keywords: zebrafish, nanoplastic, antioxidant-oxidant, polystyrene

Oral Presentation-25

Relationship between Radio Frequency Electromagnetic Field Exposure and Developmental Pathways to Obesity in Zebrafish Embryos

Derya Cansiz

Biochemistry Department, School of Medicine, İstanbul Medipol University, İstanbul, Turkiye

Obesity in children and adolescents has reached global epidemic proportions in recent years, accompanied by a rapid increase in the use of information and communication technologies. It is known that there is a significant increase in obesity not only in adults but also in children. Researchers suggest factors such as nutrition, lifestyle, and environmental conditions as the reasons for this, but they also see radio frequency electromagnetic field (RF-EMF) generation from technological devices as a significant factor.

One major causative factor for the insulin resistance and hyperglycemia associated with diabetes is obesity. In light of this information, we conducted various studies. We established a setup where we exposed zebrafish to RF-EMF during the embryonic period and examined the effects of EMF on the development of obesity in zebrafish. These studies consist of two stages. In the first stage, we applied RF-EMF exposure to zebrafish embryos for different durations. As part of the second step, we exposed zebrafish embryos to RF-EMF and then watched what might happen to pathways related to obesity in embryos.

As a result of our study, we revealed that RF-EMF exposure causes developmental defects and oxidative damage in zebrafish embryos and may increase the risk of developing obesity.

Keywords: obesity, Oxidative stress, zebrafish embryo, Electromagnetic field

Oral Presentation-26

Differential Effects of Vitamin K1 and Vitamin K1 on Zebrafish Embryogenesis

Semanur Isikoglu[1], Zulal Mizrak[1], Merih Beler[1], Gizem Egilmezer[1], Efruz İrem Akkus[2], Ismail Unal[3], Derya Cansiz[3], Ebru Emekli Alturfan[4]

[1]Marmara University, Institute of Health Sciences, Department of Biochemistry, Turkiye
[2]Istanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Medical Biology, Turkiye
[3]Istanbul Medipol University, Faculty of Medicine, Department of Biochemistry, Turkiye
[4]Marmara University, Faculty of Dentistry, Department of Basic Medical Sciences, Turkiye

The two forms of vitamin K that are found naturally are phylloquinone (vitamin K1) and menaquinone (vitamin K2). Vitamin K is known as the antihaemorrhagic vitamin and is beneficial in both treating and preventing bone and vascular disease. There is also strong evidence that it also has a role in the neurological system. Vitamin K2 functions in electron transport to prevent apoptosis, oxidative stress, and microglial activation in neuron cells. Its inhibitory effects on inflammation and α-synuclein fibrillization in Parkinson's disease have been found recently, in addition to its protective effect on cognitive functioning. With its external development, the zebrafish embryo is a suitable organism for the study of embryogenesis. The role of vitamin K in embryogenesis is also important due to its role in vitamin K carboxylation reactions via the vitamin K-dependent enzyme, γ-glutamyl carboxylase.

The aim of our study is to evaluate the effects of Vitamin K1 and K2 on developing zebrafish embryos. Zebrafish embryos were exposed to 1 and 10 µM vitamin K1 and vitamin K2 and developmental parameters, mortality rates, hatching rates and locomotor activities were analyzed. Vitamin K1 and K2 exerted differential effects on the development of zebrafish embryos depending on concentration.

The findings of our study are important in terms of providing data on the role of vitamin K in embryogenesis, especially in neurogenesis.

Keywords: Vitamin K1, vitamin K2, embryogenesis, zebrafish embryos

Oral Presentation-27

Evaluation of rs1244378045, rs767450259 and rs750556128 Mutations in Terms of Polymorphism in Diabetic Obese and Non-Diabetic Obese Individuals

Saadet Busra Aksoyer Sezgin[1], Sermin Durak[2], Faruk Celik[3], Varol Guler[1], Aysegul Sarikaya[1], Umit Zeybek[3]

[1]Faculty of Medicine, Department of Medical Biology and Genetics, Istanbul Yeni Yuzyil University, Istanbul, Turkiye
[2]Faculty of Medicine, Department of Medical Microbiology, Istanbul University Cerrahpasa, Istanbul, Turkiye
[3]Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkiye

Obesity is among the important healthcare issues that is becoming more prevalent around the world caused by adipose tissue and is linked to increased diabetes and insulin resistance. The Tumor Necrosis Factor (TNF)-Alpha overexpression in adipose tissue plays important roles in mediating obesity and insulin resistance. Tumor-Necrosis Factor-Related Apoptosis-Inducing Ligand (TRAIL), TNF family member, is an effect on the development of obesity and diabetes.

The rs1244378045, rs767450259 and rs750556128 polymorphisms of TRAIL, were evaluated with the Real-Time Polymerase Chain Reaction Method in the study.

It was found that the T-Allele of the rs767450259 had protective roles against diabetic obesity. It was shown that carrying the A-Allele in the genotype distribution of TRAIL rs750556128 polymorphism might increase the risk of obesity in diabetic patients by 1.3-fold.

Our study is the first to investigate these polymorphisms in diabetic obese and non-diabetic obese groups and will make significant contributions to the literature.

Keywords: Obesity, diabetes, polymorphism, TRAIL

Oral Presentation-28

Impaired CB1 Receptor Function and Endocannabinoid Disruption Enhance Simvastatin-Induced Skeletal Muscle Toxicity

Hilal Kalkan[1], Elisabetta Panza[2], Ester Pagano[2], Giuseppe Ercolano[2], Claudia Moriello[1], Fabiana Piscitelli[1], Mónika Sztretye[3], Raffaele Capasso[4], Vincenzo Di Marzo[5], Fabio Arturo Iannotti[1]

[1]Endocannabinoid Research Group, Institute of Biomolecular Chemistry, National Research Council, Pozzuoli, NA 80078 Italy.
[2]Department of Pharmacy, University Federico II of Naples Italy, Naples, Italy.
[3]Department of Physiology, Faculty of Medicine, University of Debrecen, 4032 Debrecen, Hungary.
[4]Department of Agricultural Sciences, University of Naples Federico II, Via Università 100 80055 Portici, Italy.
[5]Institut Universitaire de Cardiologie et de Pneumologie de Québec and Institut Sur la Nutrition et Les Aliments Fonctionnels Centre NUTRISS, Université Laval, Quebec City, QC G1V0A6 Canada.

Statins are the most prescribed lipid-lowering agents. Their use is safe, although muscular toxicity occurs in 1 in 10.000 patients. The endocannabinoid system (ECS) is a complex modulatory system involved in fine-tuning cell responses to intrinsic and extrinsic stimulants through a complex cascade of receptor activation, substrate mobilization, and enzyme reactions. In particular, the synthesis on demand of the two lipid mediators, anandamide (AEA) and 2-arachidonoylglycerol (2-AG), followed by the activation of two specific metabotropic receptors, cannabinoid receptor 1 (CB1) and 2 (CB2), is the foremost mechanism through which the ECS regulates a variety of physiological and pathophysiological processes in our body. Despite the acknowledged importance of the ECS and the potential use of cannabinoid-based drugs to treat numerous human disorders, little is known about the implication of this system in skeletal muscle diseases. Thus, the involvement of ECS in skeletal muscle disorders is of great interest due to its potential future therapeutic implications.

Based on this background, we aimed to understand the role of the ECS in simvastatin-induced myotoxicity in both murine C2C12 and skeletal muscle tissues of C57BL/6 mice, and human primary myoblasts.

We demonstrated that simvastatin-induced myotoxicity in murine myoblasts and skeletal muscle tissues is associated with the dysregulated expression of miRNAs causing repression of the Cnr1/CNR1 gene expression along with parallel inhibition of downstream PKC/ERK-mediated intracellular signaling pathways coupled CB1 receptor activation. Also, we identified the CB1 receptor's dysregulated expression and impairment of its downstream signaling pathways as a novel pathological mechanism involved in statin-induced myopathy.

Keywords: Statins, Endocannabinoid System, Muscular Toxicity, Simvastatin-induced Myotoxicity, miRNAs and PKC/ERK Signaling Pathways, Skeletal Muscle Disorders

Oral Presentation-29

Impact of IFNAR1 Gene Variations on Epilepsy: Interaction of Carbamazepine and Levetiracetam in Treatment Outcomes

Kubra Cigdem Pekkoc Uyanik[1], Zeynep Gizem Todurga Seven[2], Erhan Rasit Agay[3]

[1]Department of Medical Biology, Medical Faculty, Haliç University, İstanbul, Turkiye
[2]Department of Medical Pharmacology, Cerrahpasa Faculty of Medicine, Istanbul University-Cerrahpasa, İstanbul, Turkiye
[3]Department of Medical Pharmacology, Cerrahpasa Faculty of Medicine, Istanbul University-Cerrahpasa, İstanbul, Turkiye; Republic of Turkiye Ministry of Health, Sinan Sipahi Family Health Centre, İstanbul, Turkiye

Epilepsy is a chronic noncommunicable disease of the brain that affects around 50 million people worldwide. Impaired regulation of the activation and resolution of inflammatory cells and molecules in injured neuronal tissue represents a critical factor in the development of epilepsy. However, the precise manner in which this unbalanced regulation of inflammation contributes to epilepsy remains unclear. Consequently, one of the primary objectives in epilepsy research is to identify and elucidate the interconnected inflammatory pathways in systemic and neurological disorders that may further contribute to the progression of epilepsy.

Currently available antiepileptic drugs like carbamazepine and levetiracetam were found to exhibit anti-inflammatory effects. Our study aimed to examine the relationship between IFNAR1 gene variations as a risk factor in epilepsy patients using carbamazepine and levetiracetam drugs and their response to their clinical parameters.

Targeted next-generation sequencing (tNGS) was used to perform molecular genotyping analysis of the IFNAR1 genes in genomic DNA from 20 epilepsy patients using carbamazepine and levetiracetam drugs.

We detected rare and common variations. Our results demonstrate that variations in the IFNAR1 gene can contribute to modifications in epilepsy progression.

Keywords: Next-generation sequencing, IFNAR1, single nucleotide polymophism, genetic variation

Oral Presentation-30

Investigation of LEP, LEPR Variants, and LEP Methylation in Knee Osteoarthritis

Yasemin Oyaci[1], Dicle Rotinda Ozdas Sevgin[2], Mustafa Pehlivan[3], Demirhan Diracoglu[2], Fatima Ceren Tuncel[1], Sacide Pehlivan[4]

[1]Institute of Graduate Studies in Health Sciences, Istanbul University, Istanbul, Turkiye
[2]Department of Physical Medicine and Rehabilitation, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkiye.
[3]Department of Hematology, Basaksehir Cam and Sakura City Hospital, Istanbul, Turkiye
[4]Department of Medical Biology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkiye.

Knee osteoarthritis (KOA), also known as a degenerative disease of the knee joint, is usually the result of wear and progressive loss of articular cartilage. Leptin (LEP) is a molecule with pleiotropic functions that plays a role in the regulation of immune and inflammatory responses, hematopoiesis, angiogenesis, reproduction, bone formation, response to hypoxia, and wound healing.

In this study, we evaluated whether LEP 2548G/A and LEP receptor (LEPR) 668 A/G variants cause susceptibility in patients with KOA. In addition, methylation of CpG sites located at -31 and -51 nt of the LEP gene was examined. One hundred twenty-seven KOA patients and 93 healthy controls were included in the study. Analysis of LEP 2548G/A and LEPR 668 A/G variants was performed by PCR-RFLP method. LEP gene -31 and -51 nt methylation was performed using the MS-PCR method after bisulfite modification.

The AA genotype of the LEP 2548G/A variant was significantly more common in patients with high VAS pain scores (p=0.048), while the GG genotype was more common in patients with high BMI (p=0.020). Additionally, significantly higher unmethylation rates were observed in the -51 nt region in healthy controls (p=0.002).

Our study results show that LEP 2548G/A variant is associated with various clinical parameters such as VAS and BMI in KOA prognosis and that LEP methylation may be a risk factor for KOA development. We believe that determining LEP and LEPR gene methylation levels especially with a larger number of patients, is necessary to elucidate the relationship between leptin and KOA.

Keywords: Knee osteoarthritis, Leptin, Leptin receptor, Variant, Methylation

Oral Presentation-31

Determination of the relationship between cholinergic activity and autoimmunity in patients with Hashimoto thyroiditis

Gulten Ates[1], Ismail Cem Sormaz[2]

[1]Department of Physiology, Faculty of Medicine, Istanbul Yeni Yüzyıl University, Istanbul, Turkiye
[2]Department of General Surgery, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkiye

Background: Hashimoto Thyroiditis (HT) is an organ-specific autoimmune disease characterized by autoimmune-triggered inflammation. It is the most common autoimmune disease with a prevalence of 7.5%. The cholinergic anti-inflammatory pathway (CAP) was first described as a neural mechanism that inhibits inflammation. It has been reported that CAP creates an anti-inflammatory response by regulating the inflammatory response in various infections and autoimmune diseases. In this study, we aimed to determine the relationship between cholinergic activity in Hashimoto patients and healthy volunteers by measuring the levels of acetylcholine esterase (AChE), one of the cholinergic enzymes used as a marker of cholinergic pathway activity.

Method: AChE levels from serum of HT patients (n=12) and healty volunteers (n=12) were examined using the Enzyme-Linked Immuno Sorbent Assay method using the biotin-based double antibody sandwich method, which includes the steps of adding serum containing proteins that exhibited antigenic properties against antibodies to antibody-coated, 96-well, protein-specific kits and then adding antibodies again.The findings obtained in the study were analyzed with the Student-t test through the IBM SPSS Statistics 22 (IBM SPSS) program.

Results: AChE levels in the HT patients were significantly decreased compared to healty volunteers ($p<0.05$).

Conclusion: In our study, we observed decreased cholinergic activity characterized by decreased AChE levels in HT patients. We think that this triggers autoimmunity by causing decreased anti-inflammatory response and impaired immune tolerance, which is consistent with the literature.

Keywords: Hashimoto thyroiditis, autoimmune, cholinergic anti-inflammatory pathway, acetylcholinesterase

Oral Presentation-32

Investigation of Gene Fusions and Rearrangements in Thyroid Malignancies in the Turkish Population

Burcu Celikel[1], Gulcin Yegen[2], Nihat Aksakal[3], Semen Onder[2], S. Umit Zeybek[1]

[1]Istanbul University, Aziz Sancar Experimental Medicine Research Institue, Moleculer Medicine, Istanbul,Turkiye
[2]Istanbul University, Medicine Faculty, Medical Pathology Department,Istanbul,Turkiye
[3]Istanbul University, Medicine Faculty, General Surgery Department,Istanbul,Turkiye

Thyroid cancer is the most common endocrine malignancy. Thyroid cancers are more common especially in developed and developing countries where thyroid nodule detection and sampling are performed more frequently. Although most thyroid cancers have an indolent clinical course, their increasing incidence has led to the investigation of oncogenic changes in tumor cells and treatments targeting them. Fusion genes, known as driver or passenger mutations in many cancers, are chimeric genes that cause parts of two or more genes to join together. They may occur as a result of chromosomal rearrangements or abnormal transcription. Fusion genes have been accepted as useful biomarkers for the diagnosis of thyroid cancer and various types of cancer and the determination of target drugs, and the detected changes have been implemented for targeted treatments of patients in the clinic. Appropriate tyrosine kinase inhibitor drug treatment can be started for the patient whose gene fusion is positive. Today, many tyrosine kinase inhibitor (TKI) agents are used in various cancers such as non-small cell lung cancer, thyroid cancer and melanoma. Patients can thus benefit from targeted therapy and achieve progression-free survival and quality of life.

This study aims to explain the gene fusions and rearrangements detected in thyroid cancer and to explain the importance of tyrosine kinase-targeted therapies.

Keywords: thyroid cancer, gene fusion, tyrosine kinase, targeted therapy, inhibitor

Oral Presentation-33

SCUBE-1 as a biomarker predictor for the home follow up and hospitalization of SARS-CoV-2 patients

Mustafa Kerem Ozyavuz[1], Selcuk Eren Canakci[2], Kenan Ahmet Turkdogan[2], Faruk Celik[1], Mehmet Mesut Sonmez[3], Ibrahim Yilmaz[4], Ali Osman Arslan[5], Abdullah Emre Guner[6], Sakir Umit Zeybek[1]

[1]Istanbul University, Aziz Sancar Institute of Experimental Medicine Department of Molecular Medicine, Istanbul, Turkiye
[2]Alaaddin Keykubat University, Department of Emergency Medicine, Alanya, Antalya, Turkiye
[3]Health Sciences University, Hamidiye Sisli Etfal Training and Research Hospital, Department of Ortophedics and Travmatology, Sisli, Istanbul, Turkiye
[4]Health Sciences University, Haseki Training and Research Hospital, Department of Biochemistry, Sultangazi, Istanbul, Turkiye
[5]Bolu Abant Izzet Baysal University Medical faculty, Department of Medical Biology, Bolu, Turkiye
[6]University of Health Sciences, Hamidiye Faculty of Medicine, Department of Public Health, Turkiye

Aim: SARS-CoV-2 infection continues to be the number one health-related problem worldwide. This study aimed to determine SCUBE1 levels sensitivity and specificity.

Method: This prospective study included 100 patients aged >18 years and admitted to the emergency service due to SARS-CoV-2 infection complaint. Patients' mean age was 54.4 years, and 28 of them were women. The control group patients' mean age was 55.9±14.6 years, and 11(42.3%). Patients whose polymerase chain reaction test was positive comprised the patient group, and those with negative results constituted the control group. The patient group was divided into two subgroups: those followed up at home and those hospitalized.

Result: The SCUBE-1 level of the patients admitted to the emergency service due to SARS-CoV-2 infection was 0.16±0.08 ng/mL. While the SCUBE-1 levels did not significantly differ between groups, it significantly differed between the patient subgroups (p = 0.001). The neutrophil count (=0.001) and NLRs (p=0.010) significantly differed between the groups. The neutrophil count (p=0.003) and NLRs (p=0.015) significantly differed between the patient subgroups. The receiver operating characteristic curve analysis performed for the patient subgroups showed that the sensitivity and specificity for SCUBE-1 was 84.6% and 88.9%. The average hospital stay was 9.0 days, and a positive correlation was observed between SCUBE-1 level and length of hospital stay (p=0.007).

Conclusion: SCUBE-1 was closely related to SARS-CoV-2. In addition, SCUBE-1 may be an alternative for the biomarker gap in both home follow-up and hospitalized patients.

Keywords: Emergency Service, SARS-CoV-2, neutrophil/lymphocyte ratio, SCUBE-1

Oral Presentation-34

Comparative Evaluation of Immune Marker Expressions in Human Adipose Tissue MSCs Expressing Chimeric Cytokine Receptors

Sude Coskun[1], Alper Tunga Ozdemir[4], Rabia Bilge Ozgul Ozdemir[5], Mehmet Tolgahan Hakan[1], Nihat Aksakal[3], Ali Osman Gurol[2], Ilhan Yaylim[1], Sakir Umit Zeybek[1]

[1]Department of Molecular Medicine, Aziz Sancar Institue of Experimental Medicine, Istanbul University, Istanbul
[2]Department of Immunology, Aziz Sancar Institue of Experimental Medicine, Istanbul University, Istanbul
[3]Department of Surgery, Faculty of Medicine, Istanbul University, Istanbul
[4]Department Of Immunology, Johannes Guttenberg University, Mainz
[5]Molgen Biotechnology, Istanbul

Mesenchymal stem cells (MSCs) are early-stage cells of mesoderm development and are non-hematopoietic stem cells. MSCs can be easily isolated from bone marrow, umbilical cord, dental pulp and adipose tissue. Due to their strong immunomodulatory abilities, MSCs used in the clinic inhibit pro-inflammatory activity and trigger anti-inflammatory events. Therefore, they are promising in the regulation of immune effects for many diseases, especially autoimmune diseases. With in vitro and in vivo studies, it has been observed that MSCs suppress some immune cells. These are CD4 T cells, cytotoxic and natural killer cells, phagocytes and antigen-presenting cells and B cells. Studies have also shown that MSCs can activate regulatory T and B cells. MSCs exert their immunomodulatory effects against immune cells either through microenvironmental interactions such as cytokines, chemokines and signaling molecules also they secrete or through direct cell contact. While microenvironmental effect is provided by molecules such as HGF, TGFβ, IDO, PGE2. In addition, PD-L1, ICAM-1, CD200, and HLA-G molecules expressed on cell surfaces provide immunomodulation through cell contact. Although MSCs are promising for various diseases due to their immunomodulation abilities, the short duration of their effects is a problem. Priming MSCs with various cytokines (such as IFGγ) or environmental conditions increases their immunomodulation ability.

In order to make this effect permanent, it is aimed to ensure the continuity of the priming effect realized with IFGγ through the designed chimeric cytokine receptor. For this purpose, immune marker expressions such as IDO, TGF-β, HGF should be evaluated comparatively.

Keywords: immune markers, immunomodulatory ability, mesenchymal stem cells, priming

Oral Presentation-35

Pharmacogenomics and Its Influence on Therapy Response and Toxicity

Mahmoud Abudayyak, Gul Ozhan

Department of Pharmaceutical Toxicology, Faculty of Pharmacy, Istanbul University, Istanbul, Turkiye

Pharmacogenetics is the study of how genetic characteristics influence an individual's susceptibility to diseases and their response to medications or toxic substances.

Genetic variation can affect the drug/chemical metabolism, pharmacokinetics, and pharmacodynamics. By identifying the relationship between genetics and drug response, pharmacogenetics enables the development of personalized treatment plans that are both safe and effective, while also aiding in understanding the toxicity and side effects of chemicals and drugs. This approach is particularly valuable when designing treatment plans for cancer patients and could also play a role in treating other conditions, such as neurobehavioral disorders. As an example, ocological treatments often cause severe side effects that can disrupt therapy.

By utilizing pharmacogenetic insights, it becomes possible to determine which chemotherapeutic agents will be most effective and safe for a patient based on their genetic profile.

While recent research has significantly contributed to clinical treatment planning, further studies are needed as this field continues to evolve, in order to fully understand the connection between genetic structure and drug response.

Keywords: Pharmacogenetic, Polymorphisms, SNPs, Chemotherapeutics

Oral Presentation-36

Photodynamic Therapeutic effects of Verteporfin on foveal retinal vessels in Age-related Macular Degeneration: A year result of the retrospective study planned for three years

Ayhan Onal

Istanbul Yeni Yuzyil University

Background: Photodynamic Therapy (PDT) begins with a ten-minute intravenous infusion of light-sensitive Verteporfinin (Visudyne) for the purpose of inhibiting neovascularization (NVI), an abnormal vascular pattern, in exudative type senile macular degeneration (SMD). As seen in submacular choroidal NVI, foveal NVI occurs through the reaction between free radicals because of irradiated verteporfin, and membranes of vascular endothelial cells.

Purpose: The aims are to detect the photodynamic therapeutic effect of verteporfin on foveal retina neovascularization, apart from its outcomes of submacular choroidal NVI, and to investigate what additional contributions could provide the management of AMD.

Materials and methods: The academic content was obtained with MED LINE, EMBASE, DARE, HTA, and CRD indexes. Additionally, the data were selected from the PubMed, Google Scholar, SCOPUS, WoS, and Google Academic Papers in between 2004 and 2024. The retrospective article has been preparing since October 2023 and will have be completed by next two years.

Results: 722 eyes of a total of 600 patients with exudative AMD older than 50 years were selected. OCTA cirrus 6000 device scans were utilized.

Conclusion: Although disadvantages were faced due to difficulties in determining objective criteria, lack of long-term follow-up, the presence of second eye pathologies in selected patients, foveal retinal NVI with verteporfin was noticeable in the first one-year period of the study.

Keywords: Neovascular AMD and PDT, AMD and Photodynamic Therapy, Verteporfin and AMD, Verteporfin and Exudative AMD

Oral Presentation-37

Possible Correlations between OX40 rs17568 A/G Gene Variant and sOX40 serum levels in Gastric Cancer patients

Hajir Moosa Mohammed Al Khafaji[1,2], Ali Elselmo[3], İslim Kaleler[1,2], Dilara Sönmez[1], Mehmet Tolgahan Hakan[1], Cem Horozoğlu[4], Özlem Küçükhüseyin[1], Soykan Arıkan[5], Filiz Akyüz[6], İlhan Yaylım[1]

[1] Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Turkiye.
[2] Institute of Graduate Studies in Health Sciences, Istanbul University, Turkiye.
[3] Zonguldak Bulent Ecevit University, Faculty of Science, Molecular Biology and Genetics, Zonguldak, Türkiye
[4]Department of Medical Biochemistry, Faculty of Medicine, Halic University, Turkiye.
[5]Basaksehir Cam and Sakura State Hospital, General Surgery Clinic, İstanbul
[6]Istanbul Faculty of Medicine, Department of Gastroenterology, İstanbul

Background:

Immune checkpoint pathways, particularly OX40 (CD134) and its ligand OX40L (TNFSF4), play critical roles in regulating T-cell responses, making them promising targets for immunotherapy. This study investigates the impact of OX40 rs17568 gene polymorphism on serum levels of soluble OX40 (sOX40), and their relationship with gastric cancer risk and progression.

Methods:

A total of 173 individuals were included, comprising 88 patients diagnosed with gastric cancer and 85 healthy controls. Genetic polymorphism was assessed using Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) analysis, while serum levels of sOX40 was measured by Enzyme-Linked Immunosorbent Assay (ELISA). The association between genotype frequencies, sOX40 serum levels, clinic and histopathologic parameters were evaluated.

Results:

We found that the OX40 GG genotype was 3.7 times more frequent in gastric cancer patients compared to controls ($p < 0.001$). sOX40 levels were significantly elevated in patients, and those with the A allele showed even higher levels ($p = 0.004$). In the patients with ring cell carcinoma, the frequency of OX40 AG genotype was lower than those without it (p=0,031).

Conclusion:

As a result of our study, we believe that we were able to provide information that will contribute to the evaluation of the etiopathogenesis of the disease in the light of our data obtained as a result of examining the OX40 rs17568 genotype distributions in patients with gastric cancer, as well as the serum levels of the relevant molecules together with the histopathological data of the patients.

Oral Presentation-38

Evaluation of time-dependent molecular changes of thrombocyte concentrates prepared by apheresis method

Basma Alhamrouni Almuntasir[1], Basak Adaklı Aksoy[2], Ayca Dogan[3]

[1]Altinbas University, Faculty of Medicine, Department of Biomedical Science, Istanbul, Turkiye
[2]Altinbas University, Faculty of Medicine, Department of Pediatric Hematology, Istanbul, Turkiye
[3]Altinbas University, Faculty of Medicine, Department of Physiology, Istanbul, Turkiye

Platelet concentrates have various important roles in primary hemostasis, blood coagulation and antimicrobial resistance. Many studies in literature mainly focused on the platelet concentrate as a bacterial culture as it has a higher risk of sepsis because of the storage environment at 22± 2 C°. The aim of this study is to evaluate Attenuated Total Reflectance Fourier Transform Infrared (ATR-FTIR) spectroscopy as a new method for detecting thrombocyte concentrates molecular changes due to time. After obtaining the platelet samples in a sterile manner from apheresis platelet products, detailed spectral analysis was performed using spectra of the first, fifth and tenth days of platelet samples by ATR-FTIR spectroscopy. The results revealed that lipid and protein concentrations, protein structure and conformations and protein phosphorylation are sensitive to time factor. There were several alterations in the spectral parameters of platelet concentrates over the storage period from the first to tenth day. The results of the current study revealed the power of ATR-FTIR spectroscopy in the precise determination of time-dependent alterations in thrombocyte samples simultaneously.

Keywords: Apheresis, ATR-FTIR, blood, spectroscopy, thrombocyte.

POSTER PRESENTATIONS

Poster Presentation-01

xCT and Ferroptosis in Chemotherapy Efficacy

Ikbal Ebrar Yavuz, Ozge Sultan Zengin, Gul Ozhan

İstanbul University Faculty of Pharmacy, Department of Pharmaceutical Toxicology, İstanbul, Turkiye

The cystine/glutamate antiporter (xC), an important component of the solute carrier family 7 member 11 (solute carrier family 7 member 11, SLC7A11, xCT), is essential for maintaining cellular redox status and regulating tumour-associated ferroptosis. While xCT transports intracellular glutamate to the extracellular space, it simultaneously transports extracellular cystine into the cell, where it is converted into cysteine and incorporated into glutathione synthesis. Recent studies have shown that the overexpression of xCT, driven by various oncogenic and tumour-suppressive signalling sources, supports tumour progression and multidrug resistance by inhibiting ferroptosis through cell death pathways. Also, xCT plays a role in regulating metabolic flexibility in cancer cells, as the increased uptake of cystine leads to a heightened dependence on glutamine and glucose, resulting in reduced metabolic flexibility in cancer cells.

Despite significant advancements in the prevention, diagnosis, and treatment of cancer today, the development of multidrug resistance remains one of the most important challenges encountered in chemotherapy. Therefore, understanding the role of ferroptosis in tumour formation, progression, and treatment, as well as elucidating the factors that inhibit or activate ferroptosis, is of great importance. xCT-mediated induction of ferroptosis emerges as a key factor in the development of multidrug resistance, making xCT a promising therapeutic target.

The presentation consists of (i) the role of xCT in intracellular redox balance and ferroptosis-related cell death, (ii) the role of xCT in tumour development, drug resistance, and the nutritional dependence of cancer cells, and (iii) the development of different therapeutic strategies targeting xCT in anti-cancer treatments.

Keywords: xCT, SLC7A11, Ferroptosis, Cystine/glutamate antiporter, Drug resistance

Poster Presentation-02

Effects of Nab-paclitaxel and α-Mangostin Combination on Kinetics of Breast Cancer Cells

Ozge Ozgen[1], Idil Cetin[2], Fatmahan Atalar[3], Mehmet Rıfkı Topcul[2]

[1]Aziz Sancar Institute of Experimental Medicine, Molecular Medicine Department, Istanbul University,Istanbul Turkiye
[2]Advanced Cancer and Pharmaceutical Biotechnologies Research Unit, Faculty of Science, Department of Biology, Istanbul University, Istanbul, Turkiye
[3]Child Health Institute, Department of Rare Diseases; Department of Pediatric, Nutrition and Metabolism Unit; Istanbul Medical Faculty,Istanbul University,Istanbul Turkiye

Research in breast cancer treatment is increasingly focused on discovering innovative compounds and combination therapies that aim to improve efficacy while minimizing side effects.

This study examines both the individual and combined effects of alpha-mangostin and nab-paclitaxel on breast cancer cell lines, specifically MCF-7 and MDA-MB-231. The investigation utilizes the xCELLigence RTCA system for real-time cell index monitoring, BrdU incorporation assays to measure cell proliferation, and evaluations of mitotic activity along with caspase 3 and 7 levels to assess apoptotic responses.

Results indicate that both alpha-mangostin and nab-paclitaxel, when used alone or in combination, produce substantial anti-proliferative effects and influence cell kinetics over a period of 24 to 72 hours. Additionally, the combination therapy leads to greater cell cycle arrest and apoptosis compared to each treatment used separately.

These results suggest that alpha-mangostin may enhance the effectiveness of nab-paclitaxel, potentially enabling lower dosages in breast cancer treatments. This research offers important insights into refining therapeutic approaches and could facilitate the development of new treatment strategies in clinical settings.

Keywords: MCF-7 cell line, Nab-paclitaxel, MDA-MB-231 cell line, Alpha-mangostin, Cancer, Breast carcinoma

Poster Presentation-03

Selective Targeting of Leukemia Stem Cells by DMU-212: The Involvement of lncRNAs

Cagla Kayabasi

Balikesir University, Faculty of Medicine, Medical Biology Department, Turkiye

Leukemia stem cells (LSCs) possess the hallmark abilities of self-renewal and differentiation, similar to hematopoietic stem cells (HSCs), but undergo malignant transformation through genetic/ epigenetic alterations. LncRNAs contribute significantly to this oncogenic transformation. Resveratrol, a naturally occurring polyphenol, has been extensively studied for its chemopreventive/ chemotherapeutic properties, particularly its ability to selectively induce apoptosis in LSCs. DMU-212, a synthetic analogue of resveratrol, exhibits even more potent anti-tumor effects. This study aims to identify the lncRNAs involved in the anti-proliferative and pro-apoptotic responses of LSCs and HSCs to DMU-212 treatment.

We utilized LSC (CD34+/Oct4+/CD44+/CD133+C/D38-) and HSC (CD34+/CD117+/CD38-) cells (Celprogen) in experiments. The expression profiles of lncRNAs in cells exposed to 16.7µM DMU-212 were quantified using qRT-PCR. Bioinformatics analyses were performed using the RAIN database.

Up- and down-regulated lncRNAs identified in LSCs following DMU-212 treatment are summarized in Table1. Notably, DMU-212 had more pronounced effects on LSCs compared to normal HSCs (Figure1). Bioinformatics analyses of up-regulated lncRNAs in LSC post-DMU-212 treatment suggest distinct functional roles. Specifically, PTENP1, SNHG4, and Dio3os are predicted to inhibit the PI3K/Akt signaling pathway; Y1 is involved in cell cycle regulation; BACEAS1 induces caspase-dependent apoptosis; and TMEVPG modulates apoptosis as well as the JAK/STAT and MAPK signaling pathways. Furthermore, down-regulated lncRNAs, including MALAT1, HOTAIRM1, and HOTAIR, are implicated in the regulation of membrane potential, while DLG2AS is associated with hematopoietic cell lineage differentiation.

This study highlights the role of various lncRNAs in mediating the anti-leukemic effects of DMU-212, a compound with potential therapeutic value in selectively targeting LSCs.

Keywords: lncRNA, leukemia stem cell, hematopoietic stem cell, resveratrol analogue, DMU-212

Poster Presentation-04

Targeting PRMT5: A Promising Approach to Reverse Taxane Resistance in Castration-Resistant Prostate Cancer

Ezgi Karyemez[1], Buse Cevatemre[2], Ipek Bulut[1], Hamzah Syed[3], Ceyda Acilan[3]

[1]Graduate School of Health Sciences, Koc University, Istanbul, Turkiye
[2]Research Center for Translational Medicine, Koc University, Istanbul, Turkiye
[3]School of Medicine, Koc University, Istanbul, Turkiye

Prostate cancer (PCa) is the most common cancer type among men, and it's progression largely relies on androgen receptor (AR) signaling. Although androgen deprivation therapy (ADT) is the first-line treatment, castration-resistant prostate cancer (CRPC) among with lethal metastatic stage (mCRPC) can develop. Therefore, new therapeutic targets are needed to overcome taxane resistance.

In this study, a 'Epigenetic Drug Library' containing 150 epigenetic-targeted molecules was screened in taxane-resistant (Dtx and Cbz) CRPC cells, and the PRMT5 inhibitor (HLCL61) was identified as a candidate for reversing taxane resistance. The intracellular effects of PRMT5 inhibitors were validated by viability assays (SRB and colony formation), histone extraction, western blot, and RT-qPCR analyses.

Suppression of PRMT5 by inhibitors resulted in changes in the expression of genes that play a crucial role in the cell cycle. Resistant cells which treated with PRMT5 inhibitors demonstrated reductions in sDMA, H4R3Me2, and H3R8Me2 histone marks were observed, confirming the on-target activity of the inhibitors. Additionally, a small but significant decrease in ABCB1 mRNA levels was detected in PRMT5 inhibitor-treated cells. The reduction in Cdc25c protein levels with PRMT5 inhibitor treatment suggests that the inhibition of Cdc2-cyclin B complex phosphorylation could block the G2/M transition, thereby halting cell division.

These findings suggest that PRMT5 inhibitors offer a potential strategy for overcoming taxane resistance and may be utilized in combination therapies; however, further research is required to explore the clinical applications and safety of PRMT5 inhibitors.

Keywords: PRMT5, Chemotherapy, Drug resistance, Taxane

Poster Presentation-05

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

Merve Erkisa Genel[1], Kaan Adacan[2], Huri Dedeakayogullari[3], Remzi Okan Akar[2], Veysel Turan Yilmaz[4], Engin Ulukaya[5]

[1]Department of Medical Biology, Faculty of Medicine, Istanbul Health and Technology University, Istanbul, Turkiye
[2]Molecular Cancer Research Center (ISUMKAM),Istinye University, Istanbul, Turkiye
[3]Department of Medical Biochemistry, Faculty of Medicine, Biruni University, Istanbul, Turkiye
[4]Department of Chemistry, Faculty of Sciences, Karadeniz Technical University, Trabzon, Turkiye
[5]Department of Clinical Biochemistry, Faculty of Medicine Istinye University, Istanbul, Turkiye

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.

Keywords: Colorectal cancer, BRAF mutation, Palladium, Personalized medicine

Poster Presentation-06

Calcium Fructoborate: A Novel Natural Compound That Inhibits SIRT1 Activity

Ezgi Nur Cil, Yasemin Soysal

Dokuz Eylül University, Institution of Health Sciences, Department of Molecular Medicine, İzmir/Turkiye

SIRT1 plays important regulatory roles in many biological processes, including cellular ageing, apoptosis, sugar and lipid metabolism, oxidative stress and inflammation. Therefore, even minor alterations in SIRT1 expression and function can significantly affect cellular responses. SIRT1 inhibitors have been demonstrated to be beneficial in studies of cancer and metabolic disorders. Calcium fructoborate (CaFB) is a sugar borate ester containing organic boron and is found in plant-based foods such as celery and broccoli as vegetables and grapes and plums as fruits. CaFB has been shown to have anti-inflammatory, anti-osteoporotic, antioxidant and anti-tumor effects in in vitro studies.

In this study, the effect of CaFB, a boron compound, on SIRT1 activity was investigated by a fluorescence-based method using human recombinant Sirt1. CaFB was prepared by dissolving in assay buffer at concentrations of 2 mM, 5 mM, 10 mM, 20 mM. Fluorescence reading was performed at 360/460 nm.

According to the results, it was seen that the CaFB compound inhibited SIRT1 activity in a dose-dependent manner. CaFB significantly inhibited SIRT1 activity by 42% at a concentration of 20 mM ($p < 0.001$). The results of this study provide important and basic information.

The compound can be used as a chemical tool to elucidate the biological functions of SIRT1 and to investigate the potential therapeutic applications of SIRT1 inhibitors.

Keywords: SIRT1, SIRT1 activity, Calcium fructoborate (CaFB), Nutrition

Poster Presentation-07

Effect of Curcumin on Adipogenesis Process in 3T3-L1 Cellular Model

Ayten Darcan, Yasemin Soysal

Dokuz Eylül University, Institution of Health Sciences, Department of Molecular Medicine, İzmir/Turkiye

Obesity is a complex disease that increases the risk of many other diseases like heart and liver disease, diabetes, some cancers and cause different health problems. Adipogenesis is defined as the process of differentiation of preadipocytes to mature adipocytes. Inhibition of adipocyte differentiation can be used as a potential therapeutic strategy against adipogenesis and thus obesity. 3T3-L1 preadipocytes are widely used as an in vitro model to test adipogenesis. It is aimed to investigate the adipogenesis process in preadipocyte cells differentiated into adipocytes and to suppress the lipid increase in this differentiation process with Curcumin.

Curcumin is the key bioactive compound found in the rhizome of the turmeric plant (Curcuma longa). Curcumin, is known to have anti-oxidative, anti-adipogenic, anti-inflammatory and anti-carcinogenic properties.

Curcumin were prepared in DMSO and added to the differentiation medium (DMEM, Dex, IBMX, insulin). Different concentrations of Curcumin were added to cells seeded in 96-well plates and incubated for 48 hours.

Two days after confluency, cells were induced for differentiation with differentiation medium. Cells were differentiated into mature adipocytes on day 8. For the evaluation of differentiation and intracellular lipid accumulation in the experimental and control groups, cells were examined by Oil-Red-O staining on day 8. Then imaging was performed with an inverted microscope.

According to our WST-1 cell viability results, high concentrations of Curcumin were observed to cause cell toxicity. In conclusion, in our study with Curcumin in 3T3-L1 adipocytes, doses that can suppress lipid accumulation were observed as 25, 30, 35, 40 μM.

Keywords: Adipogenesis, Curcumin, 3T3-L1 Cellular Model, Cell Viability, Obesity

Poster Presentation-08

Investigation of Novel FOXM1 Inhibitors with in Silico, Synthesis, and In Vitro Anticancer Activity Studies

Alper Onder[1], Khaled A.n. Abusharkh[1], Venhar Çınar[2], Merve Sıkık[3], Gulce Davutlar[3], Zuhal Hamurcu[2], Mustafa Guzel[4], Mehmet Ay[1], Bulent Ozpolat[5], Ferah Comert Onder[6]

[1]Department of Chemistry, Faculty of Science, Natural Products and Drug Research Laboratory, Çanakkale Onsekiz Mart University, 17020, Çanakkale, Turkiye

[2]Department of Medical Biology, Faculty of Medicine, Erciyes University, 38039, Kayseri, Turkiye

[3]Department of Medical System Biology, School of Graduate Studies, Çanakkale Onsekiz Mart University, 17020, Çanakkale, Turkiye

[4]Research Institute for Health Sciences and Technologies (SABITA), Center of Drug Discovery and Development, Istanbul Medipol University, Kavacik-Beykoz, İstanbul, 34810, Turkiye

[5]Department of Nanomedicine, Houston Methodist Research Institute, Houston, TX 77030, USA

[6]Department of Medical Biology, Faculty of Medicine, Çanakkale Onsekiz Mart University, 17020, Çanakkale, Turkiye

Forkhead Box (FOX) protein M1 (FOXM1), a proto-oncogenic transcription factor, is overexpressed in triple-negative breast cancer (TNBC) cell lines, and plays a critical role in cell proliferation, invasion, and tumour progression, making it as a promising target for the development of targeted therapies. However, the available FOXM1 inhibitors have limited specificity, potency, and efficacy of current small molecule inhibitors against FOXM1.

Therefore, this study aimed to perform in silico, synthesis, and in vitro anticancer activity of novel potential inhibitor candidates targeting FOXM1 for the treatment of TNBC. According to our obtained results, the potential compounds were successfully synthesized and then characterized by spectroscopic methods. Molecular docking and molecular dynamics (MD) simulation studies revealed that the binding affinities of the synthesized novel inhibitor candidates for the FOXM1 DNA binding domain (DBD). The strong interactions such as hydrogen bond with the key amino acids including Asn283, His287, and Arg286 were determined. ADMET analysis were calculated in the expected range. In vitro anticancer activity studies on TNBC cell lines of the synthesized novel compounds showed that all compounds exhibited highly strong cytotoxicity in the increasing concentrations compared to the known FOXM1 inhibitor.

These findings suggest that these synthesized novel compounds may be promising FOXM1 inhibitor candidates for further in vivo animal studies.

Acknowledgement: This study was supported by The Scientific and Technological Research Council of TÜRKİYE (TÜBİTAK) ARDEB-1001 SBAG (Project No: 221S682)

Keywords: Cancer, cell signaling, inhibitor, synthesis, anticancer activity, in silico

Poster Presentation-09

In Silico, Synthesis and Biological Evaluation Studies of Novel Compounds as Dual Therapeutics for Alzheimer's Disease and Cancer Therapy

Kadircan Ural[1], Merve Sıkık[1], Alper Onder[2], Khaled A.n. Abusharkh[2], Mehmet Ay[2], Ferah Comert Onder[3]

[1]Department of Medical System Biology, School of Graduate Studies, Çanakkale Onsekiz Mart University, 17020, Çanakkale, Turkiye

[2]Department of Chemistry, Faculty of Science, Natural Products and Drug Research Laboratory, Çanakkale Onsekiz Mart University, 17020, Çanakkale, Turkiye

[3]Department of Medical Biology, Faculty of Medicine, Çanakkale Onsekiz Mart University, 17020, Çanakkale, Turkiye

Alzheimer's disease (AD) is a neurodegenerative disease associated with decreased activity of the cholinergic system in the brain. Acetylcholinesterase inhibitors (AChEI) successfully increase the concentration of acetylcholine (ACh) in the brain, leading to increased cholinergic transmission and thus cognitive function. Although there are drugs that can be used in the clinic, more effective inhibitors need to be developed because the disease cannot be completely prevented.

Therefore, this study aimed to design, synthesis and characterization of novel and potentially effective pyrano indole derivatives as potential AChE inhibitors. It was aimed to conduct detailed computational studies as a result of examining the intermolecular interactions effective between protein and ligand using molecular docking and MD simulation studies. The structures of the synthesized compounds were confirmed by FT-IR, 1H and 13C NMR and LC-MS/MS spectroscopic analysis. In vitro enzyme activity assays were performed to assess the inhibitory effects of the synthesized indole-derived compounds against AChE.

The results demonstrated that the synthesized compounds exhibited significant enzyme inhibition with high IC50 values compared to known inhibitor tacrine. Additionally, the synthesized compounds showed significant cytotoxicity on breast and colon cancer cell lines in the increasing doses for 72h treatments.

These findings suggest that the synthesized pyrano indole derivatives are promising candidates for further studies as dual therapeutics for AD and cancer diseases.

Acknowledgement: This study was supported by Çanakkale Onsekiz Mart University Research Coordination Unit (Project No: THD-2024-4682).

Keywords: Alzheimer's disease, Cancer, synthesis, inhibitor, enzyme inhibition, in silico

Poster Presentation-10

Investigation of the Effect of the HIF Signaling Pathway on the Development of Sepsis and ARDS

Nurettin Onur Kutlu[1], Ilhan Yaylim[2], Tolgahan Hakan[2], Islim Kaleler[2], Dilara Sonmez[2], Roya Mashadiyeva[2], Cem Horozoglu[3]

[1]PICU, Health Science University, Başakşehir Çam ve Sakura City Hospital, Istanbul, Turkiye
[2]Department of Molecular Medicine, Istanbul University Health Sciences Institute, Aziz Sancar DETAE, Istanbul, Turkiye
[3]Department of Biochemistry, Haliç University, Istanbul, Turkiye

Aim: The aim of this thesis was to investigate the interaction of HIF-1 alpha and HIF-2 alpha proteins on VE-cadherin, which is an important intercellular junction protein in the endothelium, and the relationship between endothelial dysfunction and capillary leakage in sepsis and the clinical picture developing in patients with capillary leak syndrome (CLS).

Methods: Blood mRNA gene expression of HIF-1 alpha, HIF-2 alpha and VE-cadherin proteins by RT-PCR and serum protein levels of HIF-1 alpha, HIF-2 alpha and VE-cadherin proteins by RT-PCR and ELISA methods were studied in blood samples obtained from sepsis/ARDS cases and control cases. The study included 40 cases with a new diagnosis of Sepsis between the ages of 1 month and 18 years who were followed up in two paediatric intensive care units with tracheal tube or tracheostomy and 30 control cases.

Results: Fifteen (42.5%) of the 40 cases in our study group were found to be compatible with the criteria for CLS. There was a general suppression of HIF-1 and HIF-2 alpha gene expression, but this suppression was not found to be significant when compared with the control group. However, serum levels of HIF-1, HIF-2 and cadherin were lower compared to control healthy children.

Conclusion: In our study, we found low levels of VE-cadherin in patients with CLS, but this low level did not show an inverse correlation with the theoretically expected increase in HIF-1 alpha and HIF-2 alpha gene expressions. Our findings are important for emphasising that VE-cadherin is an important factor in capillary leak syndrome.

Acknowledgments: This study was funded by Scientific Research Projects Coordination Unit of Istanbul University. Project number TDK-2021-37951

Keywords: Sepsis, HIF-1 alpha, fate, capillary leak syndrome

Poster Presentation-11

Detection of Lactobacillus plantarum Isolates with High Transformation Efficiency

Neslihan Akarsu[1], Remziye Nalcacıoglu[2], Ali Osman Kılıc[3], Zihni Demirbag[2]

[1] Department Of Biotechnology, Faculty of Science, Karadeniz Technical University, Trabzon/Turkiye
[2] Department Of Biology, Faculty of Science, Karadeniz Technical University, Trabzon/Turkiye
[3] Department of Medical Microbiology, Faculty of Medicine, Karadeniz Technical University, Trabzon/Turkiye

Lactobacillus bacteria belong to the order Lactobacillales, which consists of functionally related but phylogenetically distinct bacteria. They are Gram-positive, facultatively anaerobic, non-spore-forming bacteria that are capable of fermenting a wide range of sugars into lactic acid. Especially commensal Lactobacillus species are abundant in nutrient-rich mucosal membranes and foods. Therefore, they play an important role in defense against pathogenic microorganisms by being present in various human microbiomes. In addition, Lactobacillus bacteria are GRAS (generally recognized as safe) bacteria that increase resistance to infections and are effective in regulating immunity. They have significant potential in biotechnological and therapeutic applications and are among the ideal vector hosts for heterologous gene expression. Examples include the development of probiotic treatments and in situ production of mucosal vaccines. However, difficulties in genetic engineering and biotransformation of Lactobacillus species limit their potential use.

In this study, plasmid vectors (pTRK892 and pMSP3535) that can be used for cloning and expression purposes were transformed into 14 different L. plantarum isolates from local and food sources by electroporation method. Transformation efficiencies of cells were calculated and transformation results were confirmed by PCR.

As a result of the studies, it was determined that L. plantarum TLB 544 bacterial isolate had the highest transformation efficiency with values of 3.5X102 and 4X102 for the pTRK892 and pMSP3535 vectors used, respectively.

Keywords: LAB, Lactobacillus, electroporation, transformation efficiency

Poster Presentation-12

Investigation of Interactions of Mesenchymal Stem Cell-Derived Exosomes in Leukemia Cell Lines

Beyzanur Deniz[1], Ayse Mine Yılmaz Goler[2], Betul Yilmaz[2], Semra Demokan[1]

[1]Department of Basic Oncology,Oncology Institute, Istanbul University,Istanbul,Turkiye.
[2]Department of Basic Medical Sciences,Biochemistry, Faculty of Medicine, Marmara University,Istanbul,Turkiye.

Mesenchymal Stem Cells(MSCs) are a group of stem cells with multipotent properties that can be found in many tissues. They can create resistance to traditional cancer treatments and play a role in tumor growth and metastasis. The role of exosomes derived from MSCs in cancer pathogenesis and prognosis hasnot been fully elucidated yet.

In this study, the effect of exosomes derived from mesenchymal stem cells on K562, a type of chronic myeloid leukemia (CML) and HL60, an acute myeloid leukemia (AML) cell line, has been investigated. K562 and HL60 cell lines, as well as exosomes, were co-cultured at different concentrations and different time points. The cell growth profile in these cultures was determined, and cell viability,necrosis,apoptosis,and cell cycle ratios were determined.Based on the results obtained,effective genes were identified using bioinformatic methods based on gene expression levels in the cell lines.As a result of the studies,a decrease in the viability of K562 cell line and an extension of the G0/G1 phase in the cell cycle were observed,while an increase in the viability of HL60 cell line and an extension of the S and G2/M phases were observed.After co-culture,it was observed that MSC-Exo have inhibitory effects on cell proliferation in chronic CML cancer line,may promote apoptosis, and slow down the cell cycle, while they increased cell proliferation in the acute promyelocytic leukemia cell line.

Consequently, it was observed that exosomes could have different effects due to molecular characterization differences in cell lines. Target genes that could serve as biomarkers were identified through gene expression analysis.

Keywords: Exosome, leukemia, mesenchymal stem cell, HL60

Poster Presentation-13

Investigation of the Role of Adiponectin on AMPK Expression in the H9c2 Cell Line

Ulku Balandiz, Minel Can Ekin, Ozlenen Simsek Papur

Dokuz Eylül University, Health Science Institute, Department of Molecular Medicine, İzmir

Diabetic Cardiomyopathy (DCM) refers to abnormalities in the structure and function of the myocardium resulting from diabetes. In a healthy heart, there is a balance between the use of fatty acids and glucose as energy sources. In the presence of DCM, the intake of long-chain fatty acids increases in a way that disrupts this balance. CD36 facilitates the uptake of long-chain fatty acids at the plasma membrane in the heart and skeletal muscles. Fatty acid uptake is increades by the CD36 pathway in DCM. GLUT4 is a glucose transporter that mediates the uptake of glucose into the heart. AMPK is responsible for the contraction-induced translocation of CD36 and is important for the contraction-induced translocation of GLUT4. The activation of AMPK non-selectively stimulates both glucose and long-chain fatty acid uptake. Adiponectin is a hormone that can be found in plasma and enhances insulin sensitivity. In rats with adiponectin resistance, the phosphorylation processes of insulin signaling pathway proteins are disrupted, and GLUT4 translocation is inhibited.

The aim of this study is to determine the effect of adiponectin on the DCM by examining the changes in AMPK synthesis. The cardiac characteristics of H9c2 cells were confirmed through immunohistochemical staining, followed by fluorescence microscopy imaging of muscle-specific desmin intermediate filaments, cardiac-specific myosin, and perinuclear Atrial Natriuretic Factor.

DCM was mimicked in cardiac in vitro cell models and experiment were made with different concentration level of adiponectin at 30 minute and 1 hour to examine the expression change of AMPK by Western Blot.

Keywords: Adiponectin, Diabetic Cardiomyopathy, AMPK, H9c2 cell line

Poster Presentation-14

Comparison of the Cytotoxic Effects of Calcium Fructoborate and Boric Acid as Boron Compounds

Ezgi Nur Cil, Yasemin Soysal

Dokuz Eylül University, Institution of Health Sciences, Department of Molecular Medicine, İzmir/Turkiye

Boron is an essential mineral that plays an important role in many biological processes in human nutrition. One of these compounds is calcium fructoborate (CaFB), a boron derivative. The main source of CaFB, one of the organic molecules containing sugar borate, is plant-based nutrients. Natural boron compounds called sugar borates are found in commonly consumed vegetables, fruits, seeds and nuts. In previous studies, different boron compounds were investigated in adipocyte cells. Our experiments are the first to show the effects of CaFB on viability of 3T3-L1 cells.

We aimed to investigate the cytotoxic effects of the CaFB and boric acid (BA) compounds on 3T3-L1 adipocyte cells using WST-1 test. Preadipocytes in the differentiation phase were exposed to varying concentrations of boron (CaFB up to 20 mM and BA up to 1 mg/ml) in the differentiation mix. At the end of 48 hours, WST-1 analyses of adipocytes exposed to boron were performed by spectrophotometric measurement. Our results show that CaFB is safer and better tolerated by cells than BA. Even at the maximum CaFB dose (20 mM), the viability was 87%. It was found that 500 and 1000 µg/mL BA significantly reduced cell viability (68%, 65%, respectively).

As a conclusion, the CaFB compound can be used safely in obesity-related adipogenesis studies without causing toxic effects on cells at specified doses. Our findings provide data that may be the basis for further adipogenesis and obesity experiments.

Keywords: Adipocyte, Boric acid, Calcium fructoborate, Nutrition, Obesity, WST-1

Effects of 1,25-dihydroxyvitamin D3 and progesterone on T cell subsets in the pathogenesis of type 1 diabetes mellitus

Pinar Kasapoglu[1], Ali Osman Gurol[1], Gunnur Deniz[1], Suzan Adin Cinar[1], Nilgun Isiksacan[2], Temel Yilmaz[3]

[1]Department of Immunology, Institute of Health Sciences, Istanbul University, Istanbul, Turkiye
[2]Department of Biochemistry, Hamidiye Medical Faculty, University of Health Sciences,Istanbul, Turkiye.
[3]Department of Internal Medicine, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkiye

Immunologically, T1DM is a complex disease characterized by a decrease in TREG, an increase in autoreactive cells, and ultimately beta cell damage, under the influence of genetic and environmental factors.

In this study, by determining the roles of T cell subsets and especially TREG, TFH, TFR cells in the pathogenesis of diabetes of ten new-onset, fifteen previously diagnosed diabetes patients and fifteen healthy individuals, it is aimed to evaluate the effects of vitamin D and progesterone on these cells and to contribute to clinic in terms of personalized cell therapy. TREG (CD4+CD25+CD127-CXCR5-), TFH (CD4+CD25-CXCR5+), TFR (CD4+CD25+CD127-CXCR5+) was analyzed with flow cytometry before culture (fresh blood) and after anti-CD3+anti-CD28, anti-CD3+anti-CD28+vitamin D, anti-CD3+anti-CD28+progesterone, anti-CD3+anti-CD28+vitamin D+progesterone stimulations. IL-10, TGF-β, IL-21, IL-17, IL-4, TNF-α, IFN-γ levels were measured from culture supernatant.

IFN-γ, TNF-α, IL-21 levels were found to be high in all groups than control. IL-21 levels were decreased to control levels with the stimulations. IL-10 levels especially were increased with vitamin D+progesterone stimulation than the other stimulations. The TFR level of diabetic patients was found to be lower and the TFH rate was higher than the control group.

Compared to other stimulations, vitamin D+progesterone stimulation increased TFR levels and decreased TFH levels. Vitamin D had a positive effect on immune system cells in terms of autoimmunity, and this effect was strengthened by the progesterone. With these stimulations, autologous cell therapy seems to be promising in the clinic.

Keywords: Diabetes mellitus, Regulatory T cell, Follicular helper T cell, Vitamin D, Progesterone

Poster Presentation-16

Knock-down of Indoleamine 2,3-dioxygenase 1 (IDO-1) via RNAi Inhibits Proliferation and Clonogenicity of Human Breast Cancer Cells

Venhar Cinar [1,2], Zuhal Hamurcu[1,2], Gizem Bulut[3], Mehmet Tolgahan Hakan[4], Dilara Sonmez Zor[4], Islim Kaleler[4], Gultekin Isayeva[4], Ozlem Kucukhuseyin[4], Hayriye Arzu Ergen[4], Cem Horozoglu[5], Ceylan Hepokur[6], Umit Zeybek[4], Sidar Bagbudar[7], Soykan Arikan[8], Nihat Aksakal[9], Mustafa Tukenmez[9], Engin Ulukaya[3], Bulent Ozpolat[10,11], Ilhan Yaylım[4]

[1]Faculty of Medicine, Department of Medical Biology, Erciyes University, Kayseri, Turkiye
[2]Betül-Ziya Eren Genome and Stem Cell Center, Erciyes University, Kayseri, Turkiye
[3]Istinye University, Faculty of Medicine, Department of Clinical Biochemistry, Istanbul, Turkiye
[4]Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkiye
[5]Department of Biochemistry, Haliç University, Istanbul, Turkiye
[6]Department of Biochemistry, Faculty of Pharmacy, Sivas Cumhuriyet University, 58140, Sivas, Turkiye
[7]Department of Pathology, Başakşehir Çam and Sakura City Hospital, Istanbul, Turkiye
[8]Department of General Surgery, Başakşehir Çam and Sakura City Hospital, Istanbul, Turkiye
[9]Department of Endocrine Surgery, Istanbul Faculty of Medicine, İstanbul University, Istanbul, Turkiye
[10]Department of Experimental Therapeutics, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Unit 422, Houston, TX, 77030, USA
[11] Houston Methodist Neal Cancer, Houston, TX, USA

Metabolic alterations and their underlying mechanisms in cancer progression have garnered significant attention in recent years. Indoleamine-2,3-dioxygenase 1 (IDO-1), an enzyme responsible for catabolizing tryptophan (Trp) into kynurenine (KYN) and other metabolites, is notably overexpressed in various cancers such as breast cancer. Breast cancer remains one of the leading causes of cancer-related deaths among women today while most of the patients develop resistance to the present treatment approaches. Therefore, there is an urgent need to suggest new alternative strategies in clinical practice.

This study aimed to investigate the role of IDO-1 in breast cancer aggressiveness and to predict its potential as a new target. First, MCF7 IDO-1 knock-down cells were generated via RNAi. Then change in proliferation rate was measured by MTS viability assay, and the colony formation assay was performed to evaluate colonogenicity.

At the end, our findings demonstrate that knock-down IDO1 significantly decreases proliferation and inhibits colony formation in MCF-7 cells.

These results suggest that IDO-1 may promote cell proliferation in breast cancer, highlighting its potential as a novel molecular target for future therapeutic interventions aimed at proliferation inhibition.

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Keywords: IDO-1, knock-down, siRNA, MCF-7, breast cancer

Poster Presentation-17

The role of the PD-1/PD-L1 pathway in myoma

Şeyda Akın[1], Mehmet Tolgahan Hakan[2], Burçak Dilmen[3], Ceylan Hepokur[3], İlhan Yaylım[2]

[1]Sivas Cumhuriyet University, Faculty of Medicine, Department of Medical Biology, Sivas
[2]İstanbul University, Aziz Sancar Experimental Medicine Research Institute, Department of Medical Biology, İstanbul
[3]Sivas Cumhuriyet University, Faculty of Pharmacy, Department of Biochemistry, Sivas

Fibroids are benign tumors that are prevalent among women of reproductive age and exhibit a complex interaction with the immune system. In the context of fibroids, the immune system experiences both activation and suppression. An increase in specific immune cells, such as regulatory T cells and follicular helper T cells, promotes inflammatory responses, while a decrease or loss of function in cells like natural killer (NK) cells and gamma delta T cells enables tumor cells to evade immune detection. This indicates that a complex mechanism of immune regulation is involved in the pathogenesis of fibroids. Programmed cell death protein 1 (PD-1), encoded by the PDCD1 gene on chromosome 2, is a receptor located on the surface of activated T cells. When PD-1 binds to its ligand, PD-L1, it induces T cell anergy, thereby suppressing the immune response and diminishing cytokine release. This interaction facilitates the evasion of cancer cells from immune surveillance. Additionally, increased expression of PD-L1 diminishes T cell infiltration, leading to localized immunosuppression. The PD-1/PD-L1 interaction has been shown to reduce the induction of Bcl-xL, a cell survival factor, and inhibit the transition of T cells from the G1 phase to the S phase of the cell cycle. In this study, we investigated the expression levels of the PD-1/PD-L1 pathway within the complex immune regulatory mechanisms associated with fibroids. Results from quantitative polymerase chain reaction (qPCR) analysis conducted on samples from 75 patients with fibroids and 75 control individuals revealed a slight decrease in the expression of PD-1 and PD-L1 in the fibroid group compared to the control group. These findings suggest that further research is warranted to explore the role of immune checkpoint inhibitors in the pathogenesis of fibroids.

Keywords: Myoma, PD-1, PD-L1, İmmune system