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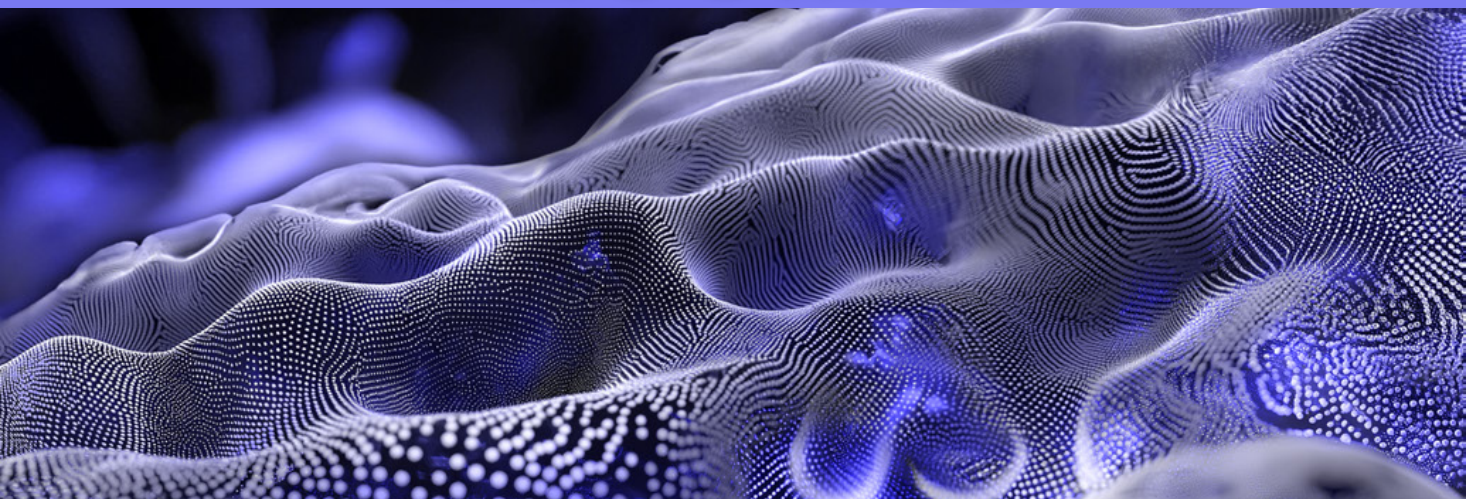
2nd INTERNATIONAL WORKSHOP *on* CANCER *and* LIPIDOMICS

Istanbul Medipol University, Türkiye

10-11 *SEP* 2024

SCIENTIFIC PROGRAM



2nd INTERNATIONAL WORKSHOP ON CANCER AND LIPIDOMICS

SCIENTIFIC PROGRAM | ***10 SEPTEMBER 2024***

08.00 - 09.30 | **Registration**

09.30 - 09.45 | **Welcome Ceremony**

09.45 - 10.45 | **Keynote Lecture** *by Besim Öğretmen*
Alterations of Ceramide Metabolism Induces PD-L1 Internalization and Resistance to Immunotherapy in Breast Cancer

10.45 - 11.30 | **Invited Speaker** *by Shikhar Mehrotra*
Targeting Thiols to Improve Anti-Tumor T Cell Therapy

11.30 - 11.50 | **Coffee Break**

11.50 - 12.35 | **Invited Speaker** *by Özgür Şahin*
From Mechanisms Of Drug Resistance To Drug Discovery

12.35 - 14.00 | **Lunch**

14.00 - 14.30 | **Invited Speaker** *by Mutay Aslan*
Plasma Sphingolipidomic Profile in Insulin Resistance and Diabetic Dyslipidemia

14.30 - 15.00 | **Invited Speaker** *by Mehtap Kutlu*
Discovering New Biomarkers for Prognosis and Treatment of Malignant Mesothelioma using LC/MS/MS

15.00 - 15.30 | **Invited Speaker** *by Yeşim Er Öztaş*
Future of Lipidomics in Clinical Diagnostics

10 SEPTEMBER 2024

15.30 - 16.30 | **Coffee Break & Poster Session**

16.30 - 17.00 | **Invited Speaker** *by Sreeparna Banerjee*
A Cross Talk Between Lipid Metabolism and Oxidative Stress in the Decision for Partial EMT in Nutrient Deprived Cancer Cells

17.00 - 17.45 | **Short Talks**
Muhammed Ali Nalbant
Relationship of Breast Cancer and Renin Angiotensin System Through ACE Gene Polymorphisms

Oğuzhan Köse
Characterization of PD-L1+ B Cell Subtypes in the Tumor Microenvironment of NSCLC

17.45 - 19.00 | **Meet The Lecturers**

19.00 | **Dinner** *(Invited Speakers)*

11 SEPTEMBER 2024

10.00 - 10.30 | **Invited Speaker** *by Mesut Bilgin*
Quantitative Shotgun Lipidomics: A Powerful Tool for Decoding Lipid Metabolic Disorders

10.30 - 11.00 | **Invited Speaker** *by Onur Çizmecioğlu*
Characterization of Cholesterol Biogenesis and PI3K Crosstalk for the Treatment of Anti-Hormone Therapy-Refractory Cancers

11.00 - 11.20 | **Coffee Break & Poster Session**

11 SEPTEMBER 2024

11.20 - 11.50 | **Invited Speaker** *by Mehmet Koçak*
Recent History of Cancer Mortality in Turkiye

11.50 - 12.50 | **Flash Talks** *by Nihan Verimli*
Targeted Destruction of Micro-Tumors: A Novel Hybrid Theranostic Agent Utilizing Gold Nanoparticles and Photodynamic Therapy

12.50 - 14.00 | **Lunch**

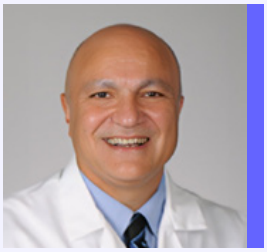
14.00 - 14.30 | **Invited Speaker** *by Serdar Durdağı*
Developing Deep Learning Models for Predicting Ligand-Protein Interactions: Integrating Protein-Ligand Conformations with Directed Message Passing Neural Networks

14.30 - 15.00 | **Invited Speaker** *by Melis Kartal Yandım*
Mcl-1 Modulation and Lipidomic Alterations: A Shotgun Lipidomics Approach in Acute Myeloid Leukemia

15.30 - 16.30 | **Coffee Break & Poster Session**

16.30 - 17.00 | **Invited Speaker** *by Jason Pierce (Online)*
Lipidomics Shared Resources: Synthesis and Analytical Core

17.00 - 18.00 | **Round Table Discussion - Concluding Remarks**



PROF. DR. **BESİM ÖĞRETMEN**

Medical University of South Carolina (MUSC), Director of Lipidomics Center, USA

10 SEPTEMBER 2024 | 09.45 - 10.45

"ALTERATIONS OF CERAMIDE METABOLISM INDUCES PD-L1 INTERNALIZATION AND RESISTANCE TO IMMUNOTHERAPY IN BREAST CANCER"

Programmed death-ligand 1, PD-L1 (CD274) facilitates immune evasion and exerts pro-survival functions in cancer cells. Here, we report a new mechanism whereby internalization of PD-L1 in response to alterations of bioactive lipid/ceramide metabolism by ceramide synthase 4 (CerS4) induces sonic-hedgehog (Shh) and TGF- receptor signaling to enhance tumor metastasis in triple-negative breast cancers (TNBC), exhibiting immunotherapy resistance. Mechanistically, data showed that internalized PD-L1 interacts with an RNA-binding protein Caprin-1 to stabilize Shh/TGFBR1/Wnt mRNAs to induce -catenin signaling and TNBC growth/metastasis, consistent with increased infiltration of FoxP3+ T regs and resistance to immunotherapy. While mammary tumors developed in MMTV-PyMT/CerS4-/- were highly metastatic, targeting the Shh/PD-L1 axis using Sonidegib and anti-PD-L1 antibody vastly decreased tumor growth and metastasis, consistent with the inhibition of PD-L1 internalization and Shh/Wnt signaling, restoring anti-tumor immune response. These data, validated in clinical samples and databases, provide a mechanism-based therapeutic strategy to improve immunotherapy responses in metastatic TNBCs.

Prof. Dr. Besim Ogretmen is associate dean of "Research, College of Medicine" and "Basic Science, Hollings Cancer Center" at Medical University of South Carolina (MUSC) from 2021. Additionally, he is the director of the "Lipidomics Facility" at MUSC from 2016. Dr. Ogretmen is also founder and chief executive officer of "Lipo-Immuno Tech" from 2021.

His research focuses are primarily on defining the mechanistic roles of sphingolipid metabolism on cancer pathogenesis and therapeutics for about 20 years, and they have developed novel molecular, pharmacologic, and genetic tools to uncover mechanisms by which sphingolipids regulate cancer growth, metastasis, and anti-cancer therapeutics. Additionally, he has developed a very strong "Lipid Signaling in Cancer Program" and "Lipidomics Shared Resource" at Hollings Cancer Center (HCC), which he serves as director. He also served as the director and the principal investigator of the Center of Biomedical Research Excellence (P30, COBRE) in Lipidomics and Pathobiology at MUSC.

In addition, he has been involved in the building up the cancer research team, which has been key for the NCI-redesignation of their Cancer Center in 2014. Furthermore, he has been the PI for a Program Project Grant (P01, PPG), which focuses on targeting lipid signaling for cancer therapy, including a phase II clinical trial.

PROF. DR. **SHIKHAR MEHROTRA**

Medical University of South Carolina (MUSC), USA

10 SEPTEMBER 2024 | 10.45 - 11.30

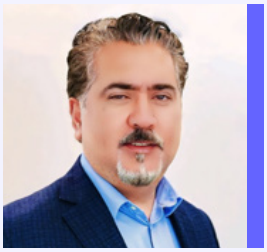
"TARGETING THIOLS TO IMPROVE ANTI-TUMOR T CELL THERAPY"

Improving persistence and sustained function of effector T cell response is key for achieving significant tumor control in adoptive T cell immunotherapy protocols. Our studies have shown that high anti-oxidant property is central to potent anti-tumor effector T cells, and directly correlates to central memory (Tcm), low glycolytic and low mitochondrial membrane potential phenotype, all of which may be linked and contribute to better tumor control. We have also shown that Tcm cells exhibit a relative increase in the expression of cell surface thiols (c-SH), a key target of cellular redox controls, along with other antioxidant molecules. Additionally, over-expressing cystathionine β-synthase (Cbs), an enzyme involved in the biosynthesis of endogenous H2S – that promoted c-SH, stemness, antioxidant capacity and exhibited increased protein translation mediated in part by Peroxiredoxin-4. In in vivo models of melanoma and lymphoma, anti-tumor T cells conditioned ex vivo with exogenous H2S or overexpressing Cbs demonstrated superior tumor control upon adoptive transfer. These data suggest that antioxidant levels regulate the efficacy of ACT, by mitigating tumor induced organelle stress that could potentiate T cell anti-tumor capacity.

Prof. Dr. Shikhar Mehrotra is professor of "Department of Surgery" and "the Cecilia and Vincent Peng Endowed Chair in Melanoma and Cutaneous Oncology" at Medical University of South Carolina (MUSC). He is also co-leader of "Cancer Immunology Program" in Holings Cancer Center at MUSC. Additionally, he is co-founder and chief scientific officer of "Lipo-Immuno Tech".

His research has mainly focused on understanding T-cell signaling and metabolic pathways for improving cancer immunotherapy. His lab is testing several strategies to generate tumor-reactive T-cells that can persist longer and lead to control of tumor growth, and they have previously described a novel approach to demarcate effector T-cells based on cell surface thiol (c-SH) expression into c-SHhi and c-SHlo T cells. In his recent study, he demonstrated that the levels of sphingosine-1-phosphate (S1P), a known pro-survival lipid, can be a determinant in T cell effector vs. regulatory phenotype.

Furthermore, he has successfully obtained NIH R41, R21, and RO1 funding in the past as an independent investigator.



PROF. DR. ÖZGÜR ŞAHİN

Medical University of South Carolina (MUSC), USA

10 SEPTEMBER 2024 | 11.50 - 12.35

"FROM MECHANISMS OF DRUG RESISTANCE TO DRUG DISCOVERY"

Breast cancer is the most commonly diagnosed cancer and the leading cause of cancer death in women worldwide. It is a highly heterogeneous disease, and clinically classified into three subtypes: estrogen receptor-positive (ER+), HER2-positive (HER2+) and triple negative breast cancer (TNBC). Depending on the subtype, breast cancer patients can be treated with different targeted therapy, immunotherapy and chemotherapy agents. However, a large fraction of patients exhibits disease recurrence and metastasis, greatly reducing the clinical outcome. Our main goal has been to elucidate the molecular mechanisms of cancer therapeutics, drug resistance, and metastasis in most aggressive breast cancers by conducting cutting-edge interdisciplinary research. We are also interested in developing and pre-clinical testing of novel anti-cancer therapeutics that are easily translatable to clinics. In our lab, we develop and utilize state-of-the- art tools, e.g., cancer cell lines sensitive or resistant to various standard of care therapies, patient-derived xenografts (PDXs), transgenic animal models, organoids (both PDX- and patient-derived) in combination with cutting-edge transcriptomics/proteomics methods to answer key questions in drug resistance and metastasis. In this talk, I will discuss the contribution of the structural elements (e.g., ECM) as well as different immune cell types to resistance to chemotherapy and/or targeted therapy agents in highly aggressive breast tumors. Furthermore, I will show the examples of using our in-house developed/clinically tested inhibitors to overcome resistance to standard-of-care therapies used in breast cancer treatment. These exemplary studies show outstanding dedication of our lab to translating our benchwork to clinics for the most aggressive breast cancers for the benefit of patients.

Prof. Dr. Özgür Şahin is tenured professor and SmartState Endowed Chair in the Department of Biochemistry & Molecular Biology and Hollings Cancer Center at Medical University of South Carolina (MUSC). He is also founder and president of LoxiGen.His laboratory mainly focuses on elucidating the mechanisms of cancer therapeutics, drug resistance and metastasis. Furthermore, they are in the process of translating the findings to the clinics for treatment-refractory ER+ patients.

Previously, he held positions as a research team leader in the Division of Molecular Genome Analysis at DKFZ, as a research faculty in the Department of Molecular & Cellular Oncology at the University of Texas MD Anderson Cancer Center (MDACC), as an assistant professor in the Department of Molecular Biology & Genetics at Bilkent University and as an associate professor in the Department of Drug Discovery & Biomedical Sciences at University of South Carolina.

In addition, Dr. Sahin was an EMBO-YIP Installation Grant Awardee and later American Cancer Society Research Scholar. He also has received multiple funding for (as PI) for his research from the EMBO, European Union FP7 Program, TUBITAK, American Cancer Society and the National Institutes of Health. Dr. Sahin has received many awards, including TUSEB Aziz Sancar (Nobel Laureate) Science Incentive Award from the Health Institutes of Turkey, Outstanding Young Scientist (GEBIP) Award from Turkish Academy of Sciences, USC Research Excellence Award, and MUSC Research Excellence Award.

PROF. DR. MUTAY ASLAN

Akdeniz University, Antalya, Türkiye

10 SEPTEMBER 2024 | 14.00 - 14.30

"PLASMA SPHINGOLIPIDOMIC PROFILE IN INSULIN RESISTANCE AND DIABETIC DYSLIPIDEMIA"

Obese patients with type 2 diabetes (T2DM) have increased plasma ceramides (CER), associated with insulin resistance and inflammation. A persistent CER elevation results in excessive ceramide deposition in the muscles of obese individuals with T2DM. Ceramide accumulation 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.

We have reported a significant decrease in insulin resistance (HOMA IR) accompanied by a decrease in serum levels of C24 SM, C22-C24 CERs, and C1P in morbid obese patients following laparoscopic sleeve gastrectomy (LSG) at 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.

In a separate 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. C24:C16 SM and C24:C16 CER ratio showed a significant correlation with both LDL-C and non HDL-C levels.

In conclusion, serum long chain CERs, C24:C16 SM, C24:C16 CER ratio may serve as prognostic and diagnostic markers in type 2 diabetic dyslipidemia.

Prof. Dr. Mutay Aslan graduated from Cukurova University Faculty of Medicine and completed her medical residency training at Akdeniz University Faculty of Medicine. She received her Ph.D. in Biochemistry and Molecular Genetics from the University of Alabama at Birmingham in the United States. She is working as a laboratory supervisor at Akdeniz University Hospital and is also a lecturer at Akdeniz University Faculty of Medicine in Turkiye. She also serves as a member and was in the Management Committee of EU-COST. In addition, she has been an independent expert/evaluator for the European Commission in selection of research proposals and has also been elected to the Advanced Courses Committee of The Federation of European Biochemical Societies (FEBS) in January 2021 for a four-year term.

Currently, Dr. Aslan continues her work in the Research and Diagnostic Lab at the Department of Medical Biochemistry at Akdeniz University. In recent years, she has intensified her studies on lipoproteins, fatty acids and sphingolipids. She has 115 publications that have been published in peer-reviewed journals and a published patent. According to Google Scholar, these publications have more than 4063 citations and the h-index is 31.

PROF. DR. MEHTAP KUTLU

Eskisehir Technical University, Eskisehir, Türkiye

10 SEPTEMBER 2024 | 14.30 - 15.00

"DISCOVERING NEW BIOMARKERS FOR PROGNOSIS AND TREATMENT OF MALIGNANT MESOTHELIOMA USING LC/MS/MS"

Malignant mesothelioma (MM) is a rare tumor with a poor prognosis arising from the mesothelial surfaces of the pleura, peritoneum, tunica vaginalis, or pericardium. Malignant pleural mesothelioma (MPM) is the most common type of MPM, accounting for approximately 81% of all cases. It is a difficult type of cancer to treat, as it is usually diagnosed at an advanced stage. After diagnosis, the average life expectancy is approximately 1 year. The two most important factors in the development of MPM are asbestos and erionite. In developing countries, asbestos exposure is increasing rapidly with the growth of the industry. The most important biomarker of MPM is mesothelin, which is moderately successful in diagnosing MPM; however, mesothelin is not reliable in individuals who have not developed mesothelioma. Therefore, new sensitive and discriminative biomarkers are needed for the diagnosis and prognosis of this disease. Recent research on cancer has focused on the relationship between sphingolipid metabolism and cancer. Ceramides are abundant in cell membranes and act as second messengers in various cellular signaling pathways. Furthermore, ceramides are powerful molecules with potential in the development of therapeutic strategies against many diseases, including cancer. Disruption of lipid metabolism may be an early biomarker for the onset of cancer. With the development of mass spectrometry and chromatographic techniques, lipidomics has become a new research area, particularly in the diagnosis and treatment of cancer. In cancer research, serum plasma and liquid biopsy samples instead of biopsy for lipidomics analyses are used as more reliable materials for the diagnosis and treatment of MPM. In this study, lipid derivatives were detected using LC/MS/MS lipidomics in the in vitro NCI-H2452 mesothelioma cell line and plasma samples obtained from patients diagnosed with MPM who received treatment and follow-up, and the obtained data were comparatively analyzed.

Prof. Dr. Hatice Mehtap KUTLU did her master's thesis on Some Serum Enzyme Activity Levels and Ion Exchange in the Blood of Patients with Type I and Type II Diabetes Mellitus at Anadolu University, Department of Biology, Molecular Biology, in 1990. She completed her PhD thesis in the same department on the inhibition of the gamma-aminolevulinic acid dehydratase enzyme of Gammarus spp. by Lead and Some Biochemical Properties in 1996. Since 2006, she has been working as a Professor at Anadolu University, Department of Biology, Molecular Biology, USA. She is currently working in the same department that was formerly a part of Eskisehir Technical University. During this period, she held administrative duties as the head of the department and vice head of the department. She has been involved in many national projects (TUBITAK, BAP) as an executive and researcher. Thus far, she has supervised 9 doctoral and 24 master's students. She teaches many courses such as Molecular Cell Physiology, Enzymology, and Biochemistry of Carcinogens and Mutagens at the undergraduate, graduate, and doctoral levels. Her research interests include sphingolipid-cancer relationship, cancer cell death pathways, flow cytometric cell death pathway analysis, electron microscopy and confocal microscopic imaging, in vitro cytotoxicity, cell culture studies, alternative cancer models, and drug research. She has published more than 100 articles in international and national peer-reviewed journals, including oral and poster presentations, and her current publications have been cited by other researchers. In addition, she has a patent from the US Patent Office on the use of ceramidase inhibitors for cancer treatment.

PROF. DR. YEŞİM ER ÖZTAŞ

Hacettepe University, Ankara, Türkiye

10 SEPTEMBER 2024 | 15.00 - 15.30

"FUTURE OF LIPIDOMICS IN CLINICAL DIAGNOSTICS"

Lipid research has developed later than its counterparts, genomics and proteomics. However, development of MS technologies and bioinformatics opened a new window for detecting a high majority of lipid species and quantifying them. Unlike nucleic acids and proteins, which have easily interpretable codes, lipids have diverse but distinct structures without such codes. They consist of various combinations of fatty acid chain lengths, differing in the number and location of double bonds, and have various functional head groups linked to glycerol or sphingoid base backbones.

Traditionally, plasma lipid panels used for diagnosing and monitoring diseases focused primarily on cholesterol levels, specifically LDL and HDL. However, the goal has now shifted towards determining the comprehensive lipid species within these particles. Advances in lipidomic technologies have enabled routine monitoring of lipid metabolism to unravel disease biology, identify improved predictive or diagnostic biomarkers, and develop new therapeutic strategies. One notable development is the high-throughput ceramide assay analyzed via LC-MS/MS, which has been adopted in clinical practice in predicting cardiovascular disease at the Mayo Clinic. The goal of clinical lipidomics is to establish new lipidomic assays that provide insights into clinical outcomes, although this is a complex process that requires regulatory approval. The Lipidomics Standards Initiative (LSI), with the assistance of the International Lipidomics Society (ILS), has compiled guidelines for minimum reporting standards, promoting standardization and harmonization in the field. The long-term goal is to make these standards a routine part of research publications and disseminated data.

Dr. Yeşim Er Öztaş is a professor of Medical Biochemistry at Hacettepe University. She completed her medical degree at Hacettepe Medical Faculty and pursued her clinical chemistry residency at Ankara Medical Faculty. Following her residency, she earned a PhD in Medical Biochemistry from the Institute of Health Sciences at Hacettepe University.

Dr. Öztaş's research primarily focuses on lipid and cell membrane biochemistry. Her laboratory has been studying lipid metabolism alterations in diseases such as sickle cell anemia and cystic fibrosis. Her contributions to the field are well recognized, with several publications in prestigious journals. Beyond her research, she served as an editor for the journal "Acta Medica" since 2013.

PROF. DR. **SREEPARNA BANERJEE**

Middle East Technical University, Ankara, Türkiye

10 SEPTEMBER 2024 | 16.30 - 17.00

"FUTURE OF LIPIDOMICS IN CLINICAL DIAGNOSTICS"

Cancer cells need to rewire their metabolism and activate both catabolic and anabolic pathways to cope with the requirements of rapid proliferation. The core of a tumor can be limiting in both nutrients and oxygen, especially with poor vasculature. Such cells induce autophagy to recycle macromolecules or degrade damaged organelles in the lysosome.

Colorectal cancer cell lines incubated in a nutrient depletion (ND) medium containing 10% of the nutrients found in complete medium (Nutrient rich, NR) showed the activation of autophagy. However, the surviving cells were highly viable and could form tumors in vivo. Since autophagy is reliant on the lysosome, we inhibited lysosomal acidification with Bafilomycin A1 (Baf) and observed a remarkable change in cell shape from cobblestone to elongated; these cells displayed markers for partial EMT (p-EMT) and motility.

To understand mechanistic underpinnings for the induction of p-EMT, we evaluated the transcriptome of Caco-2 cells grown in NR or ND +/- Baf treatment. Protein-protein interaction networks and in silico modeling suggested that cells under ND+Baf used lipid metabolism in the decision between survival and death by apoptosis. The mitochondria in these cells generated ROS; high ROS levels led to apoptosis. With lower amounts of ROS, the cells could activate the EMT program, most likely to escape from the low availability of nutrients.

Overall, our data supports the idea that cells at the core of the tumor, where nutrients and oxygen can be limiting, can activate a number of different metabolic and signaling pathways in order to survive.

Prof. Dr. Sreeparna Banerjee is a prominent figure in the field of cancer metabolism and molecular biology, currently serving as a faculty member at the Department of Biological Sciences, Middle East Technical University (METU) since 2017. She earned her Ph.D. in Food Sciences from the University of Leeds, preceded by a Master's degree from the same institution, and a Bachelor's degree in Physiology from India.

Her research primarily focuses on understanding the pathways regulating metabolism in cancer cells. Using colorectal cancer as a model, her laboratory systematically focuses on pathways related to lipid and carbohydrate metabolism and the role played by these bioactive compounds in the regulation of inflammatory pathways.

Apart from her research, Prof. Banerjee has been actively involved in academic leadership as a member of the Ethics Committee at METU's Faculty of Arts and Sciences since 2015. She also teaches several undergraduate courses, such as Biology 2, Molecular Biology Laboratory, and Cell Biology Laboratory, contributing to the education and mentorship of future scientists.

PROF. DR. MESUT BİLGİN

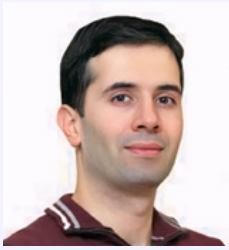
Danish Cancer Institute, Copenhagen, Denmark

11 SEPTEMBER 2024 | 10.00 - 10.30

"QUANTITATIVE SHOTGUN LIPIDOMICS: A POWERFUL TOOL FOR DECODING LIPID METABOLIC DISORDERS"

The intricate balance of lipid metabolism plays a crucial role in various physiological processes, and its disruption is implicated in numerous disorders, including cancer. My talk will focus on advancing lipid metabolic profiling through innovative methodologies. Specifically, I will discuss the application of Quantitative Shotgun Lipidomics using High-resolution Mass Spectrometry to analyze lipid profiles comprehensively. This approach enables the detailed quantification of lipid species, offering deep insights into metabolic alterations associated with lipid disorders.
A significant aspect of this work involves the development and implementation of homemade tools for data processing. These tools streamline the analysis, allowing for more accurate and efficient interpretation of complex lipidomic data. By addressing challenges such as data noise and variability, these custom solutions enhance the reliability of lipidomic studies.
The talk will also introduce Tracer-Assisted Shotgun Lipidomics, a cutting-edge strategy that combines isotopic tracers with lipidomics to investigate lipid metabolism more dynamically. This approach has proven particularly valuable in revealing enzymatic mechanisms underlying cancer drug resistance. By tracing the metabolic pathways of lipids within cancer cells, this method uncovers potential targets for therapeutic intervention, offering a new dimension to understanding and overcoming drug resistance.
These approaches offer new insights into lipid metabolism, particularly in the context of disease and therapy, advancing the field of lipidomics.

Dr. Mesut Bilgin is a distinguished researcher and the driving force behind the Lipidomics Core Facility at the Danish Cancer Institute (DCI). He has been instrumental in pioneering mass spectrometry-based lipidomics methodologies since 2009. His expertise in cancer biology, particularly in understanding the role of lipid metabolism in cancer, has positioned him as a leading figure in the field.
In 2015, Dr. Bilgin advanced to the role of research leader at DCI, where he established a cutting-edge lipidomics laboratory. Under his guidance, the lab has become a hub for comprehensive lipid research, equipped with state-of-the-art mass spectrometry tools that enable the quantification of hundreds of lipid species in mammalian samples.
His research focuses on the intricate roles of lipids in disease, with a particular emphasis on cancer. He investigates the connection between obesity and cancer, examining how lipids secreted by adipocytes influence cancer cell behavior. His research is not limited to cancer alone but also extends to other disorders that are linked to obesity. He explores the impact of lipid metabolic reprogramming across several diseases, aiming to uncover underlying mechanisms and identify potential therapeutic targets.
Beyond cancer and obesity, his research group collaborates extensively with over 20 research teams worldwide, exploring the role of lipids in a variety of diseases and biological processes. His commitment to advancing lipidomics research continues to push the boundaries of our understanding of lipid biology and its impact on health and disease.



ASSIST. PROF. **ONUR ÇİZMECİOĞLU**

Bilkent University, Ankara, Türkiye

11 SEPTEMBER 2024 | 10.30 - 11.00

"CHARACTERIZATION OF CHOLESTEROL BIOGENESIS AND PI3K CROSSTALK FOR THE TREATMENT OF ANTI-HORMONE THERAPY-REFRACTORY CANCERS"

PTEN loss and PIK3CA mutations are the most prevalent PI3K pathway changes that cause cancer. PIK3CA activating mutations lead to p110α dependence, and p110β becomes the prominent PI3K isoform upon PTEN loss. In this talk, we aimed to share our insight on the molecular mechanisms of PI3K dependence upon PTEN loss and PIK3CB overactivation. For this purpose, we analyzed GEO datasets of tumor models induced by either activated PI3K3CB or PTEN loss. Several gene set enrichment analyses revealed that PI3K activation upregulated metabolic pathways and fine-tuned the cholesterol and steroid biogenesis. Among the upregulated genes, SQLE is highly amplified in tumor samples as a rate-limiting enzyme. Concomitantly, mRNA levels of cholesterol synthesis pathway enzymes were directly correlated with PI3K activation status in microarray datasets and diminished upon PTEN re-expression in PTEN-null castration resistant prostate cancer cell lines. Particularly, PTEN re-expression decreased SQLE protein levels in PTEN-deficient prostate cancer cell lines. We performed targeted metabolomics and detected reduced levels of cholesteryl esters as well as free cholesterol upon PTEN re-expression. Of note, PTEN-null breast and prostate cancer cell lines were more sensitive to pharmacological intervention with the cholesterol pathway than PTEN-replete cancer cells. Consequently, CRPC cells exhibited an increased level of sensitivity upon simultaneous inhibition of cholesterol biosynthesis and the androgen receptor. According to our data, the cholesterol synthesis pathway could constitute a metabolic vulnerability for PTEN loss-driven cancers, and we speculate that this strategy has the potential to treat anti-hormone therapy refractory breast and prostate cancers.

Assist. Prof. Onur Çizmecioğlu graduated from the Department of Molecular Biology and Genetics at Bilkent University in 2002. He received his Ph.D. degree in 2009 from the German Cancer Research Center (DKFZ) and Heidelberg University in cell biology. During his PhD and a subsequent concise post-doctoral training in the laboratory of Prof. Ingrid Hoffmann, he conducted research in the fields of cell cycle and centrosome duplication. His efforts in the Hoffmann lab culminated in publication of key first and/or second author research articles in prestigious journals including The Journal of Cell Biology, The EMBO Journal, Journal of Biological Chemistry, Journal of Cell Science and Cell Cycle. In order to gain expertise in signal transduction and cancer biology, he joined the lab of Prof. Thomas M. Roberts at Dana-Farber Cancer Institute (DFCI), Harvard Medical School as a research fellow in 2011. His research at DFCI elucidated unique and redundant features of phosphoinositide 3-kinase (PI 3-kinase) isoforms in regulation of signal transduction and carcinogenesis and resulted in two additional publications in Oncogene and eLIFE (and one other under revision). In September 2016, Dr. Çizmecioğlu returned to his Alma mater and joined the ranks of the Department of Molecular Biology and Genetics as an assistant professor. His current research is centered on how different members of PI 3-kinases are involved in signaling and cancer.

PROF. DR. MEHMET KOÇAK

Istanbul Medipol University, Istanbul, Türkiye

11 SEPTEMBER 2024 | 11.20 - 11.50

"RECENT HISTORY OF CANCER MORTALITY IN TURKIYE"

To increase the awareness of cancer disease burden in a given population, we have to first understand the dynamic nature of diagnostic and prognostic profiles of these diseases. Such disease profiles are dynamic not only over time but over demographics and geographies as well. As we understand better where we were, where we currently are, and where we project to be in any of the cancer diagnosis and prognosis, we then expect to be able to plan and develop timely and effective health policies to increase access to disease prevention, treatment, and rehabilitation services. In this talk, we first present a global outlook of cancer epidemiology and projections. We then focus on the recent history of cancer-related mortality in Turkiye overall and in a province-specific manner to illustrate the above-mentioned dynamic nature of disease burden. We also illustrate another layer of complexity in this dynamic structure as age and gender health disparities in addition to the geographic disparities. The natural next steps for such epidemiological research pursuits are to initiate investigations aiming to identify the contributors/causes to the observed variability of the disease burden such as socio-demographics factors, environmental markers, behavioral traits, etc. Only though these steps can we propose sociodemographic and geography specific health policies and services.

Prof. Dr. Mehmet Koçak is a professor of Biostatistics in the International School of Medicine at Istanbul Medipol University, and he is the chair of the department of biostatistics and medical informatics and the director of Biostatistics and Bioinformatics Analysis Unit. He earned his MSc degree in applied statistics from Michigan State University, and a PhD in applied statistics from the University of Memphis. Furthermore, he has been a study biostatistician for numerous Phase-I and Phase-II brain tumor clinical trials conducted by St. Jude Children's Research Hospital from 2002-2011, and by Pediatric Brain Tumor Consortium (PBTC) from 2002-2021. He joined the Department of Preventive Medicine at the University of Tennessee Health Science Center (UTHSC) in 2011, and supported clinical and observational studies conducted by UTHSC.

His areas of research have been time-course gene expression data analysis, meta-analysis of p-values, Phase-I/II clinical trial design, survival analysis, and categorical data analysis. He is an expert in SAS programming language as well as Statistical Simulations and Graphics.

PROF. DR. **SERDAR DURDAĞI**

Bahçeşehir University, Istanbul, Türkiye

11 SEPTEMBER 2024 | 14.00 - 14.30

"DEVELOPING DEEP LEARNING MODELS FOR PREDICTING LIGAND-PROTEIN INTERACTIONS: INTEGRATING PROTEIN-LIGAND CONFORMATIONS WITH DIRECTED MESSAGE PASSING NEURAL NETWORKS"

Prof. Dr. Serdar Durdağı is a professor and dean of School of Pharmacy at Bahcehir University. He earned his MSc degree in from Bilkent University, and a PhD in from the Free University of Berlin.

His primary focus is on developing effective computational techniques that enable a deeper understanding and exploration of these interactions. In recent years, his laboratory has been dedicated to developing novel codes using machine learning approaches to develop structure- or ligand-based models against different diseases.

In addition, He received several prestigious awards including the Turkish Academy of Sciences (TÜBA) Academy Award and TUBA Academy Medal (2023); The Scientific and Technological Research Institution of Turkiye (TUBİTAK) Incentive Award (2016); Science Academy BAGEP award (2014); Health Institutes of Türkiye (TUSEB) Aziz Sancar Incentive Award (2017); BAU Respect for Science Awards - Contribution to Science Award (2017); BAU Respect for Science Awards - Contribution to Society Award (2021); and BAU Respect for Science Awards - Contribution to Science Award (2023); and BAU 25th Year Special Science Award (2023).
He is also the Ambassador of the Biophysical Society (BPS) of Türkiye for the term of 2024-2026.

ASSIST. PROF. MELİS KARTAL YANDIM

Danish Cancer Institute, Lipidomics Core Facility &
Izmir University of Economics, Izmir, Denmark

11 SEPTEMBER 2024 | 14.30 - 15.00

"MCL-1 MODULATION AND LIPIDOMIC ALTERATIONS: A SHOTGUN LIPIDOMICS APPROACH IN ACUTE MYELOID LEUKEMIA"

Acute Myeloid Leukemia (AML) is an aggressive hematological malignancy that presents significant clinical challenges due to limited treatment options and often unfavorable outcomes.
Mcl-1 is an anti-apoptotic protein commonly overexpressed in AML cells, contributing to their resistance to traditional chemotherapy. Mcl-1 inhibitors have emerged as a potential therapeutic breakthrough, aiming to disrupt the protective mechanisms that AML cells use to escape apoptotic signals. S63845 is a small molecule inhibitor of Mcl-1 with high binding affinity.
Bioactive sphingolipids are critical signaling molecules involved in various cellular processes, including proliferation, death, and senescence. Altered intracellular sphingolipid levels are known to contribute to chemotherapy resistance. Additionally, targeting sphingolipid metabolism has been suggested as an alternative therapeutic approach in cancer, potentially leading to Mcl-1 downregulation.
In light of this information, modulation of both Mcl-1 and sphingolipid metabolism may synergistically alter the lipidome of the cells, initiating the signaling pathways for cell death.
In this talk, we will present the results of our research study, which aimed to observe changes in lipid profiles via quantitative shotgun lipidomics in response to dual targeting of Mcl-1 and sphingolipid metabolism in AML cell lines, and discuss our future perspectives.

Assist. Prof. Melis Kartal Yandım pursued her master's and doctoral studies at the Department of Molecular Biology and Genetics, İzmir Institute of Technology, earning her master's degree in 2010 and her PhD in 2015. Following her doctoral studies, she conducted postdoctoral research at the same department between February 2015 and April 2016. From 2009 to 2015, she served as a Research Assistant at the Department of Molecular Biology and Genetics at İzmir Institute of Technology. She has been a faculty member in the Department of Medical Biology at the Faculty of Medicine, Izmir University of Economics since 2016.

Her research interests include cancer molecular biology, mechanisms of multidrug resistance, sphingolipid metabolism, apoptosis mechanisms, drug repurposing, and combination therapies.

In 2022, she worked as a Visiting Scientist at the Danish Cancer Institute's (Kræftens Bekæmpelse) ""Cell Death and Metabolism"" and ""Lipidomics Core Facility"" groups for two months. She then continued in this role for 12 months from 2023 to 2024. During this period, she was supported by TUBİTAK2219 Fellowship Program.