Taiwan-Lithuania Joint Biotechnology Research Symposium

22 September
2023 Vilnius

NSTC 國家科學及技術委員會
National Science and Technology Council

Research Council of Lithuania

Agenda

Taiwan-Lithuania Joint Biotechnology Research Symposium

Venue: Life Sciences Center, 7 Saulėtekio Ave, Vilnius
Auditorium: R401 (4th floor)

September 22, 2023

08:30-09:00 Registration

09:00-09:10 Opening Addresses
Dr. Gintaras Valincius, Chairman of the Research Council of Lithuania
Dr. Yi-Juang Chern, Deputy Minister, NSTC
Mr. Eric Huang, Head of the Taiwanese Representative Office in Lithuania

09:10-09:20 Signing of Memorandum of Understanding

09:20-09:25 Dr. Tai-Horng Young, Director-General, Dept. of Life Sciences, NSTC

09:25-09:30 ***Group Photo***

09:30-09:45 Dr. Jonathan Arias, LSC-EMBL Partnership Institute for Genome Editing Technologies at the Vilnius University Life Sciences Center: ***"Harvesting iPS cell and gene editing technologies for cell-based therapeutics and disease modelling"***

09:45-10:00 Dr. Yu-Chi Chou, Biomedical Translation Research Center, Academia Sinica: ***"Introduction to CRISPR techniques and resources in the RNA Technology Platform and Gene Manipulation Core"***

10:00-10:15 Dr. Stephen Knox Jones, LSC-EMBL Partnership Institute for Genome Editing Technologies at the Vilnius University Life Sciences Center: ***"How precise is precise? Revealing the targeting specificity of CRISPR nucleases"***

10:15-10:30 Dr. Steven Lin, Institute of Biological Chemistry, Academia Sinica: ***"Genome engineering of human natural killer cells"***

10:30-10:45 Dr. Urte Neniskyte, LSC-EMBL Partnership Institute for Genome Editing Technologies at the Vilnius University Life Sciences Center: ***„The development of delivery vectors targeting brain tissue".***

10:45-11:15 ***Coffee break***

11:15-11:30 Prof. Chia-Jui Yen, Department of Oncology, National Cheng Kung University: ***"Buildup pancreatic cancer bio information data bank and develop individual and tailor precision anti-cancer treatment"***

11:30-11:45 Prof. Dr. Feliksas Jankevičius, General Director, Vilnius University Hospital "Santaros klinikos": ***"Personalized cancer biomarkers replacing follow-up instrumental examinations and helping in difficult clinical decisions"***

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11:45-12:00 Prof. Shao-Chun Wang, Graduate Institute of Biomedical Sciences, China Medical University: ***"Developing marker-guided effective cancer therapy"***

12:00-12:15 Prof. Ming-Huang Chen, Department of Oncology, Taipei Veterans General Hospital: ***"The role of tertiary lymphoid structures (TLSs) in the tumor microenvironment of cholangiocarcinoma"***

12:15-13:30 ***Lunch***

13:30-13:45 Prof. dr. Juozas Kupčinskas, Department of Gastroenterology & Institute for Digestive Research, Lithuanian University of Health Sciences: ***"Towards personalized solutions in inflammatory and malignant digestive diseases"***

13:45-14:00 Dr. Tatjana Ivaškiene, Director of Centre for Innovative Medicine: ***"Research Activities in State Research Institute Center for Innovative Medicine"***

14:00-14:15 Assoc.Prof. You-Tzung Bob Chen, Graduate Institute of Medical Genomics and Proteomics, National Taiwan University ***"ICE CRIM mice for cancer studies" ipsum***

14:15-14:30 Prof. Yu-Ting Chang, Department of Internal Medicine, National Taiwan University : ***"Blood Biomarkers for Early Detection of Pancreatic Cancer: Opportunities and Challenges"***

14:30-14:45 Closing remarks

14:45-15:00 ***Coffee Break***

15:00-16:00 ***Excursion to the Laboratories of the Life Sciences Center***

HARVESTING iPS CELL AND GENE EDITING TECHNOLOGIES FOR CELL-BASED THERAPEUTICS AND DISEASE MODELLING

Dr. Jonathan Arias
PhD, Group of nuclease-enabled cell therapeutics
VU - EMBL partnership institute for gene editing technologies

The convergence between human iPS cells and gene editing technologies allow us to access cell types and genome configurations that are rare or normally inaccessible for disease modelling and therapeutic prototyping ex vivo. During this talk I will present developments for the creation of isogenic cell models using bi-allelic editing with CRISPR-Cas9 in a deterministic manner. I will discuss how such bi-allelic editing can be used to model neurodegeneration in Parkinson's disease and the early onset rare-disease ceroid lipofuscinosis. Furthermore, I will show how genetically encoded sensors enable the stratification of patients and facilitates compound screening with high-throughput and high-content systems.

More about the scientist
Jonathan Arias (PhD) pursues the creation of Advanced Therapeutic Medicinal Products (ATMPs) with special focus on onco-immunology and orphan diseases. His R&D leverages in the technologies of induced pluripotent stem cells (iPSC) and genome engineering.
He obtained his MSc in Karolinska Institutet (Sweden) and PhD in Kyoto University (Japan). He conducted two post-doctoral fellowships in Karolinska Institutet (Sweden) and University of Oslo (Norway). He is author of 15 scientific articles in the field of regenerative medicine and genome engineering. He is inventor on 3 granted patents, one of them in genome engineering. He is lecturer on graduate courses in Karolinska Institutet and Vilnius University. He is an active member of the innovation ecosystem. He founded the Arias lab at VU - EMBL in 2022 and currently host 9 scientists and graduate students.

"I believe regenerative medicine and genome engineering will drive next generation therapeutics. Jonathan Arias"

INTRODUCTION TO CRISPR TECHNIQUES AND RESOURCES IN THE RNA TECHNOLOGY PLATFORM AND GENE MANIPULATION CORE

Dr. Yu-Chi Chou
Associate Research Specialist
Biomedical Translation Research Center (BioTReC), Academia Sinica, Taiwan

RNA Technology Platform and Gene Manipulation Core is one of the 24 national core facilities supported by the National Core Facility for Biopharmaceuticals (NCFB) of National Science and Technology Council (NSTC). NCFB is aimed to make efficient use of the research resources and provide professional high-tech services to academic and industrial researchers in Taiwan. As the only national core facility offering comprehensive gene manipulation techniques and services, we combine various gene manipulation tools (RNAi, miRNA, CRISPR/Cas and cDNA reagents) with multiple recombinant viral delivery systems (lentivirus, retrovirus and AAV), and provide valuable technical supports for all biomedical researchers in academia, medicine and industry. The emerging CRISPR/Cas genome editing technology is one of the core technologies currently under development. We have collected a variety of currently available Cas proteins and compared their capabilities in genome editing. Several in-house R&D related to gene manipulation have been conducted to improve core technology and service quality. Using a combined treatment of small molecule compounds (NHEJ inhibitors, HDR enhancers, p53 inhibitors, cell cycle blockers, chromatin modifiers), We have increased the gene knock-in efficiencies up to 90% by homology-directed repair in certain cell lines (HEK-293T, HeLa and C33A). We also developed dual-AAV systems which carry split Cas9s (base-editors or prime-editors) and split GFPs for the use of in vivo genetic engineering, which have been demonstrated to successfully correct the disease SNPs in cell and mouse models. To increase the AAV targeting specificity for the gene therapy, AAV peptide display libraries with millions of engineered AAV capsid variants were generated for the development of targeted gene transfer AAV vectors. The emerging technology and service platform established by this core facility can not only meet the needs of academic research, but also support the R&D of the biomedical industry in Taiwan.

More about the scientist
Yu-Chi Chou received the MSc and PhD degrees in the Institute of Microbiology and Immunology (Majoring in Virology) at 1998 and 2004, respectively, from the National Yang Ming University. After post-doctoral training in the Institute of Molecular Biology at Academia Sinica (Taiwan), Dr. Chou joined the RNAi core facility (recent the RNA technology platform and gene manipulation core), where he is now the manager of the national core facility (since 2015). Dr. Chou is a research specialist of the Biomedical Translation Research Center (BioTReC) at Academia Sinica (since 2016) and a contract associate research fellow of the Department of Medical Research at Taipei Veterans General Hospital, Taiwan (since 2020). With deep expertise in gene manipulation and virus preparation, the national core facility led by Dr. Chou is committed to advancing scientific knowledge in Taiwan through introducing emerging technologies and providing customized services. More than 2,000 research teams in Taiwan (including academia and biomedical R&D departments) have requested core services, with a total of 15,000 service applications. Those services have assisted Taiwanese researchers in publishing more than 2,200 papers in SCI journals. During the COVID-19 pandemic, Dr. Chou and his team have made significant contributions to the development of national COVID-19 vaccines (MVC-COV1901 and UB-612). In order to fulfill the needs of academic and industrial researches, Dr. Chou and his team have continuously introduced emerging CRISPR/Cas technology to provide technical supports for R&D, which is of great benefit to the biomedical development (e.g., gene therapy and cell therapy) in Taiwan.

HOW PRECISE IS PRECISE? REVEALING THE TARGETING SPECIFICITY OF CRISPR NUCLEASES

Dr. Stephen Knox Jones
Research Professor & Group Leader
EMBL Partnership Institute at the Vilnius University Life Sciences Center

Genome editing tools transform scientists into authors, capable of rewriting genomes to match our research, diagnostic, and therapeutic needs. A decade of precision genome editing with CRISPR nucleases has exposed a clear imperative for our next generation of editing tools: We must increase their safety while continuing to expand their application space.
Targeting specificity – a nuclease's ability to cut an intended DNA target while ignoring all other 'off-target' DNA – defines a key safety parameter for evaluating these powerful tools. By performing high-throughput kinetic profiling of CRISPR nucleases, we show that engineering efforts typically improve targeting specificity. Yet, when broadening a nuclease's potential targets can also increase its off-targets. Our profiling also enables us to predict how nucleases like Cas9 and Cas12a function in different genomes, and it informs what we should seek in our next generation of genome editing tools.

More about the scientist
Dr. Stephen Jones is from the United States, where he earned his doctorate in Molecular Biology, Cellular Biology and Biochemistry at Brown University with Dr. Richard Bennett. He produced his postdoctoral research in CRISPR biochemistry and cellular aging with Dr. Ilya Finkelstein at the University of Texas. There, he developed high throughput strategies for uncovering and benchmarking the targeting specificity of CRISPR nucleases.
In 2021, Stephen moved to Lithuania to become a founding group leader of the EMBL Partnership Institute for Genome Editing Technologies at Vilnius University's Life Sciences Center. He leads his group in their search to discover and characterize CRISPR nucleases and other enzymes for genome editing. This year, Stephen became Lithuania's first winner of the European Research Council's Starting Grant.

GENOME ENGINEERING OF HUMAN NATURAL KILLER CELLS

Dr. Steven Lin
Assistant research fellow
Institute of Biological Chemistry, Academia Sinica, Taiwan

Cell immunotherapy is a promising strategy to treat cancers. Natural killer (NK) cells are an attractive cell type for immunotherapy because of unique cancer recognition, safe allogeneic transfer, and low risk of severe immune reactions. However, our understanding of NK cell immunology is limited and hindered by the lack of efficient genetic tools for NK cell research. The major bottleneck is that NK cells are highly sensitive to exogenous DNA such as plasmids and viral vectors, which are needed to introduce gene modifications of interest. My lab is developing CRISPR genome editing tools and recombinant viral vectors to study and modify NK cells. Our goal is to better understand the mechanisms of anti-cancer activities of NK cells. The knowledge will help develop more effective immunotherapy for solid tumors.

More about the scientist
Steven Lin received the MSc degree in Biochemistry from The Ohio State University and PhD degree in Microbiology from University of Illinois, Urbana-Champaign. He then joined Dr. Jennifer Doudna's lab in University of California, Berkeley for postdoctoral training in CRISPR genome editing. He returned to Taiwan in 2016 and established his research lab at the Institute of Biological Chemistry in Academia Sinica, Taiwan. He is interested in the genetic engineering of human natural killer (NK) cells for cancer therapy. His lab is developing CRISPR genome editing tools, modified DNA templates and viral vectors to enable robust genome modifications, viral transduction and high-throughput CRISPR screening in NK cells.

THE DEVELOPMENT OF DELIVERY VECTORS TARGETING BRAIN TISSUE

Dr. Urte Neniskyte
Senior Researcher & Group Leader
LSC-EMBL Partnership Institute, Vilnius University Life Science Center

The discovery of CRISPR/Cas systems provides new opportunities to treat different human disorders, including various neuropathologies, at the genome level. However, the advancement of gene editing therapies for human disease has been significantly lagging behind the development of relevant molecular tools, to the large part due to the lack of suitable delivery vectors for CRISPR/Cas systems in vivo. The major limitation of gene editing therapeutics, including but not limited to CRISPR/Cas tools, has long been the size of the load that can be delivered to the patient's cells. We use advanced adeno-associated viruses (AAVs) with modified capsids that can deliver the transgenes to the brain, but they are too small envelope even simple Cas9 nucleases together with their sgRNAs, thus cannot be used for advanced genome editing tools. An attractive alternative is non-replicating HSV-1 vectors that have virtually no limitations in size (their load exceeds 120 kb), allowing the simultaneous delivery of the largest gene editing tools together with their guide RNAs and any additional regulatory elements. Such HSV-derived vectors carry particular importance for the treatment of brain diseases, because they are intrinsically neurotropic and can thus efficiently deliver genome editing tools into neurons. On the other hand, we collaborate with other groups in the Center, which develop lipid-nanoparticles, and evaluate their capacity to deliver Cas ribonucleoproteins to different brain cells.

More about the scientist

Dr. Urte Neniskyte received her PhD in Biochemistry at the University of Cambridge (UK) working under the supervision of Prof. Guy C. Brown and contributing to the first studies that identified microglial phagocytosis of live neurons as one of the mechanisms of inflammatory neurodegeneration, now known as phagoptosis. Then she joined the group of Dr. Cornelius Gross at the Epigenetics and Neurobiology Unit of the European Molecular Biology Laboratory (Italy) for her post-doctoral fellowship funded by Marie Skłodowska Curie Actions to identify molecular signals that guide synaptic pruning by microglia. After returning to the Life Sciences Center of Vilnius University with another MSCA fellowship, U. Neniskyte established a Molecular Neurobiology research group. Since 2021, Urte is a group leader at Vilnius University and European Molecular Biology Laboratory Partnership Institute for Genome Editing Technologies. U. Neniskyte aims to develop CRISPR-Cas delivery system for selective gene editing of brain cells and to apply it in the models of nervous system disorders. These tools are then used to define the mechanisms that are required for the maturation of neuronal networks during brain development combining in vitro, ex vivo and in vivo approaches.

BUILDUP PANCREATIC CANCER BIO INFORMATION DATA BANK AND DEVELOP INDIVIDUAL AND TAILOR PRECISION ANTI-CANCER TREATMENT

Dr. Chia Jui Yen
Professor
Medical oncology, National Cheng Kung University, Tainan, Taiwan

National Cheng Kung University Medical Center focuses on gastrointestinal malignancy precision medicine development. Major gastrointestinal malignancy including pancreatic cancer has been well collected the delicate data banks in National Cheng Kung University Medical Center. Four fineness cancer data banks including 1) physicians provide electronic structural cancer text information 2) radiologist build up the high-resolution image data and interpretation 3) pathologist construct the digital pathology data interpretation and the tissue DNA preparing 4) bioinformatics group analysis the next generation sequence cancer genome platform. Combine all this important data information and the new anticancer drugs including the target therapy and immune checkpoint therapy, the medical team can figure out the precision treatment for personal cancer treatment strategy than increase the treatment efficacy. The study aims to build up "Gastrointestinal malignancy precision medicine decision making platform" and construct the pancreatic cancer and cholangiocarcinoma malignancy molecular pathology model. Setup the personal gastrointestinal malignancy treatment strategy and bio information bank direct clinical trial and explore the new anticancer drug mechanism in pancreatic cancer and cholangiocarcinoma malignancy. National Cheng Kung University Medical Center can upload 250 cases per year certificate high quality structural chart information, high resolution image data, digital pathology data and tumor genome data to National Center for High-Performance Computing. The information can provide to develop the exploring the novel biomarker and cancer risk model.

More about the scientist

Chia-Jui Yen obtained his MD degree from National Yang Ming University and PhD degree from Institute of Clinical Medicine from National Cheng Kung University. Currently, Dr Yen is serving as the director of the Department of Oncology and the director of Cancer Center at National Cheng Kung University Hospital. He is also a professor of oncology at the College of Medicine National Cheng Kung University, as well as a joint professor at the Clinical Medicine Institute, Basic Medicine Research Institute, and Pharmacology Institute of National Cheng Kung University.

Dr Yen main research focus on new drug development on treatment of liver cancer and gastrointestinal malignancy Dr Yen has collaborated and participated in over 60 clinical trials with international pharmaceutical companies and biotech companies in Taiwan to lead multiple clinical trials for the development of new anti-cancer drugs including novel targeted drugs and immunotherapy drugs. Especially, Dr Yen have contributed to the development of Ramucirumab, a new drug for second-line treatment of advanced liver cancer, which has been approved for health insurance coverage in Taiwan, leading to improved control of liver cancer and extension of patients' lives. Professor Yen is the principal investigator of "Establish gastrointestinal cancer biomedical databank and develop individual precision cancer treatment" with four-year project funded by the National Science and Technology Council, Taiwan. The project's research framework focuses on constructing a " Gastrointestinal malignancy precision medicine decision making platform " and establishing clinical databases for pancreatic cancer and bile duct cancer tumors at NCKU Medical Center for analysis and verification. The project will also establish electronic medical records, high-resolution image databases, digital pathology databases, and tumor gene databases. By gathering cross-disciplinary experts to provide a precise cancer treatment platform and discussions.

INTRODUCTION TO CRISPR TECHNIQUES AND RESOURCES IN THE RNA TECHNOLOGY PLATFORM AND GENE MANIPULATION CORE

Dr. Feliksas Jankevicius
Professor, Vilnius University
Director general, Vilnius University Hospital "Santaros klinikos"

Epigenetics is a promising research field provided new insights into the molecular mechanisms of cancer biology. Currently epigenetic-based cancer biomarkers have shown promise for detection, diagnosis, prognosis, and prediction of response to therapy. DNA from the original tumor can be analyzed to identify specific alterations that may serve as a "personalized" biomarker. Consequently, personalized tumor signature may be used as a blood- or urinary-based tests for early detection of cancer recurrence after curative-intent treatment and objective enhancement of decision-making about adjuvant chemo and immunotherapy after cancer surgery.

More about the scientist
Professor at Vilnius University, Feliksas Jankevicius is urological surgeon who specialises in surgery of genitourinary cancer and reconstructive urology, alongside development of molecular markers of prostate, bladder and kidney cancer. As a principal investigator he has conducted 12 clinical studies, has published over 65 PubMed-linked papers and authored several book chapters. He began his specialist urologist career at National Cancer institute in Vilnius. Subsequently, he completed five year clinical research fellowship at Heinrich-Heine University in Dusseldorf. He is currently serving as a General Director of Vilnius University Hospital Santaros Clinics and earlier (2017-2019) was appointed as a director of National Cancer Institute.
Professor Jankevicius is a member of various professional organizations including the European Association of Urology (EAU) and the German Urologic Society (DGU). He has been awarded for development of cancer biomarkers National Prize for Science and International Medal of Sapienti SAT in 2018.

DEVELOPING MARKER-GUIDED EFFECTIVE CANCER THERAPY

Dr. Shao-Chun Wang
Professor and Vice Dean, College of Medicine
Director, Research Center for Cancer Biology
Investigator and Deputy Director, Center for Molecular Medicine
China Medical University & Hospital
Taiwan, R.O.C.

Mechanism-driven molecular biomarkers and targets play a crucial role in enabling durable and effective therapeutic responses in cancer treatments. Under the leadership of Academician Dr. Mien-Chie Hung, who serves as the President of Taiwan's China Medical University (CMU), the university has successfully established an interdisciplinary research center that integrates fundamental and clinical research. This center serves as the driving force behind CMU's exploration of marker-guided effective therapy (MGET) at the forefront of cancer research. The purpose of this presentation is to provide an overview of CMU's comprehensive cancer research efforts and highlight the significant contributions made by the Research Center for Cancer Biology (RCCB). Additionally, it will showcase recent groundbreaking discoveries made by the center and discuss its growing influence in the international scientific community.

More about the scientist
Shao-Chun Wang completed his undergraduate studies at Taipei Medical University, majoring in pharmacy, obtained PhD degree in genetics and cell biology from the University of Minnesota, Twin Cities, followed by post-doctoral research at M. D. Anderson Cancer Center. In 2007, Dr. Wang embarked on his independent research career as a faculty member at the University of Cincinnati Department of Cancer Biology, where he continues to maintain an affiliation. In 2016, he was recruited back to Taiwan to join China Medical University, where he played a crucial role in leading the Center for Molecular Medicine and subsequently became the director of the newly established Research Center for Cancer Biology. Dr. Wang currently holds the positions of professor and Vice Dean at the College of Medicine within the university.

THE ROLE OF TERTIARY LYMPHOID STRUCTURES (TLSS) IN THE TUMOR MICROENVIRONMENT OF CHOLANGIOCARCINOMA

Dr. Ming-Huang Chen
Professor
Department of Oncology, Taipei Veterans General Hospital, Taipei, Taiwan

Cholangiocarcinoma (CCA) is the second most common hepatobiliary malignant tumor with poor prognosis. Recently, TOPOZ-1 study demonstrated adding durvalumab (anti-PD1 Ab) to chemotherapy (Gemcitabine and cisplatin) improved the objective response rate (ORR) and overall survival (OS). Combine immune therapy and chemotherapy becomes a new standard therapy. Our team also conducted a phase 2 investigator initial study which used nivolumab (anti-PD1 Ab) plus gemcitabine and TS1 as first-line treatment in CCA. Our results demonstrated promising ORR and OS. We identified loss of function in chromatin remodeling genes is a novel immune biomarker of CCA. In the current study, we want to further investigate another potential immune biomarker: tumor microenvironment (TME). We found that the treatment response for immunotherapy in patients with TLS has a better objective response.
Upon further investigation into the TME of CCA, we have definitively confirmed the presence of hot tumors in CCA. Additionally, we have observed significant differences in the composition of hot and cold tumor samples, particularly in the expression of B and T lineage genes. Interestingly, among the top 10 genes showing differential expression, eight belong to the B cell lineage, suggesting a strong correlation between hot tumors and tertiary lymphoid structures (TLS). To delve deeper, we employed NanoString GeoMx® Digital Spatial Profiling (DSP) Technology to compare the disparities between TLS and tumor infiltrating lymphocytes (TILs). Simultaneously, we have developed a two-gene model (CD79A and MS4A1) that accurately distinguishes CCA patients into cold or hot groups. This model addresses the limitations associated with clinically used specimens in identifying TLS. In summary, our findings confirm the presence of hot tumors in CCA, with notable variations in the expression of B and T lineage genes. The dominance of B cell lineage genes among the top differentially expressed genes underscores the significant association between hot tumors and TLS. Furthermore, our utilization of NanoString GeoMx® DSP Technology and the development of a two-gene model provide valuable insights and a practical solution for identifying TLS in CCA patients, overcoming the limitations of conventional clinical specimens.

More about the scientist
Ming-Huang Chen obtained his MD degree from China Medical University and PhD degrees from the Institute of Clinical Medicine at National Yang-Ming Chiao-Tung University in 2002 and 2013, respectively. He is currently serving as the Director of the Division of Medical Oncology, Department of Oncology at Taipei Veterans General Hospital from 2023. Additionally, he holds the position of professor at National Yang-Ming Chiao-Tung University, starting from 2021. Dr. Chen's professional focus lies in the field of medical oncology, with particular expertise in upper gastrointestinal cancer and neuroendocrine tumor. He actively engages in investigator-initiated clinical trials and translational research, aiming to bridge the gap between laboratory discoveries and clinical applications in cancer treatment.

TOWARDS PERSONALIZED SOLUTIONS IN INFLAMMATORY AND MALIGNANT DIGESTIVE DISEASES

Prof. dr. Juozas Kupčinskas
Professor, Lithuanian University of Health Sciences
Head of Gastroenterology Department & Institute for Digestive Research

Institute for Digestive Research and Department of Gastroenterology at Lithuanian University of Health Sciences are among leading research teams in the field of microbiome and cancer in Baltic countries. We are involved in multiple top-level international and national research projects and consortia in the field of gut microbiome including six ongoing Horizon projects as well as previous successful collaborations with Taiwanese counterparts. Our group focuses on molecular profiling of cancer and gut microbiome. Examples of research that will be presented during the event cover translational research in chronic inflammatory bowel disease and gastrointestinal cancer. The team of researchers at LSMU would be interested in developing common future research projects in the mutual areas of interest. Competencies of the team cover next generation sequencing, cell-sorting, bioinformatics, cell lines, organoids, etc. The group also has a large biobank of different biological gastrointestinal specimens that can be integrated in collaborative projects.

More about the scientist
Prof. Juozas Kupčinskas is the Head of the Gastroenterology Department and Institute for Digestive Research at the Lithuanian University of Health Sciences in Kaunas, Lithuania. He received his MD from the Lithuanian University of Health Sciences in Lithuania in 2009. He has completed his PhD at Otto Von Guericke University (Magdeburg, Germany) in 2012 and gained subsequent medical and research training at University of Kiel (Germany) and Rambam hospital (Haifa, Izrael). He is a Council member of European Microbiota Study Group (EHMSG) and European Association for Gastroenterology, Endoscopy & Nutrition (EAGEN). He is also a member of Scientific Committee of United European Gastroenterology (UEG). Juozas Kupcinskas is a member many international research consortia including PANcreatic Disease ReseArch (Pandora), European Microscopic Colitis Study Group (EMCG), Gastric Cancer Research (staR), and European Network for the Study of Cholangiocarcinoma and others. His main research interests are related to translational research in premalignant and malignant GI cancers, gut permeability, cfDNAs, microbiome and fecal transplantation. The team of J. Kupcinskas has experience in implementing large scale Horizon Europe and other international research projects.

RESEARCH ACTIVITIES IN STATE RESEARCH INSTITUTE CENTER FOR INNOVATIVE MEDICINE

Dr. Tatjana Ivaškiene
Director of Centre for Innovative Medicine

The presentation will cover the overview of research activities performed in Center of Innovative Medicine, incl. review of departments, main specialization areas, possible topics for collaboration. The research center specializes on biomedical research and has active international and national network of business and research partners (63 countries). Also, the licensing to perform research on all levels is present: in vitro, in vivo, preclinical, clinical. The infrastructure includes in vivo facilities, cell and tissues biobank, digital and molecular pathology infrastructure, immunotechnology and stem cells research infrastructures. In recent years (2018 - 2022) 80% of papers are published in Q1/Q2 journals (CA WoS). The center provides specialized open-access laboratories and equipment for life sciences, individual services (research protocols for your personal needs, experiments based on your requirements and specification) and the possibility to do joint R&D projects together with our researchers. The State Research Institute Center for Innovative Medicine is open for collaboration.

More about the scientist
Ph.D. Tatjana Ivaskiene is currently acting as a General Manager of the State Scientific Institute Centre for Innovative Medicine. She is a board member of the National Health Board and an expert at the European Medicines Agency in the field of advanced therapy medicinal products, a member of the European Regulatory Affair Committee and EU Market Access & Value Committee at Alliance for Regenerative Medicine. Her areas of interest are advanced therapy medicinal products, cell & gene therapies, and regulatory science, translational medicine. Her initial background is in medicine, which was later enriched with law studies, pharmacy, and executive MBA.

ICE CRIM MICE FOR CANCER STUDIES

Assoc.Prof. You-Tzung Bob Chen
Associate Professor
National Taiwan University, Graduate Institute of Medical Genomics and Proteomics

Somatic mutagenesis to create specific cancer gene mutant variants in situ is not a feasible research approach before the CRISPR/Cas9 gene editing technology and the next generation sequencing (NGS) analysis are available. Here we described an inducible Cas9 effector/CRISPR mutagen (ICE CRIM) mouse model to perform somatic mutagenesis on the well-known Trp53 tumor suppressor gene, and two key players, Mlh1 and Msh2, in DNA mismatch repair (MMR). In our model, we observed global MMR deficiency accelerated Trp53 mutant-driven hematopoietic neoplasm development. MMR deficient tumorous tissues displayed a microsatellite instability (MSI) phenotype. A common hypothesis for MMR deficiency-caused tumorigenesis is the accumulation of frame-shift mutations in the coding mononucleotide repeat (cMNR) of downstream cancer gene targets. Due to the genome sequence differences in mouse and human, the MSI targets are not identical in the two species thus raise the discussion on the conservation of the causes of MMR-deficient tumor development. We used a customized probe capture technology to enrich for the mouse counterpart of the human MSI-targeted cMNRs in tumors for NGS analysis. Our results suggest a conservation on the MMR deficiency-caused tumorigenesis between the two species.
Other than developing tool mice for in vivo functional genomics studies, we are also applying the latest CRISPR/Cas9-derived genome editing techniques to correct mutations in diseased iPSCs from patients with inherited hematopoietic disease such as G6PD deficiency, and neurodegenerative disease such as PKAN or MPAN. We aim to build in vitro disease models (and their isogenic controls) using these euploid human iPSCs as well as to explore the possibility of developing gene therapeutic means for them.

More about the scientist
You-Tzung Bob Chen received his BSc and MSc from Department of Zoology, National Taiwan University (NTU). He went to US and received Ph.D. degree from Prof. Allan Bradley's laboratory at Baylor College of Medicine in 2003. His postdoctoral training was performed in Prof. Richard Behringer's laboratory at UT MD Anderson Cancer Center (2003-2008). Bob is currently an Associate Professor in NTU College of Medicine with adjunction appointments to Centers of Genome and Precision Medicine, Center for Developmental Biology and Regenerative Medicine, and Center of Biotechnology Development in NTU. His group is using both the traditional genetic manipulation techniques, as well as the latest CRISPR/Cas9-derived technologies to construct tools for functional genomics studies and potential applications in translational medicine. Platforms used in his lab include transgenic mice and pluripotent stem cells.

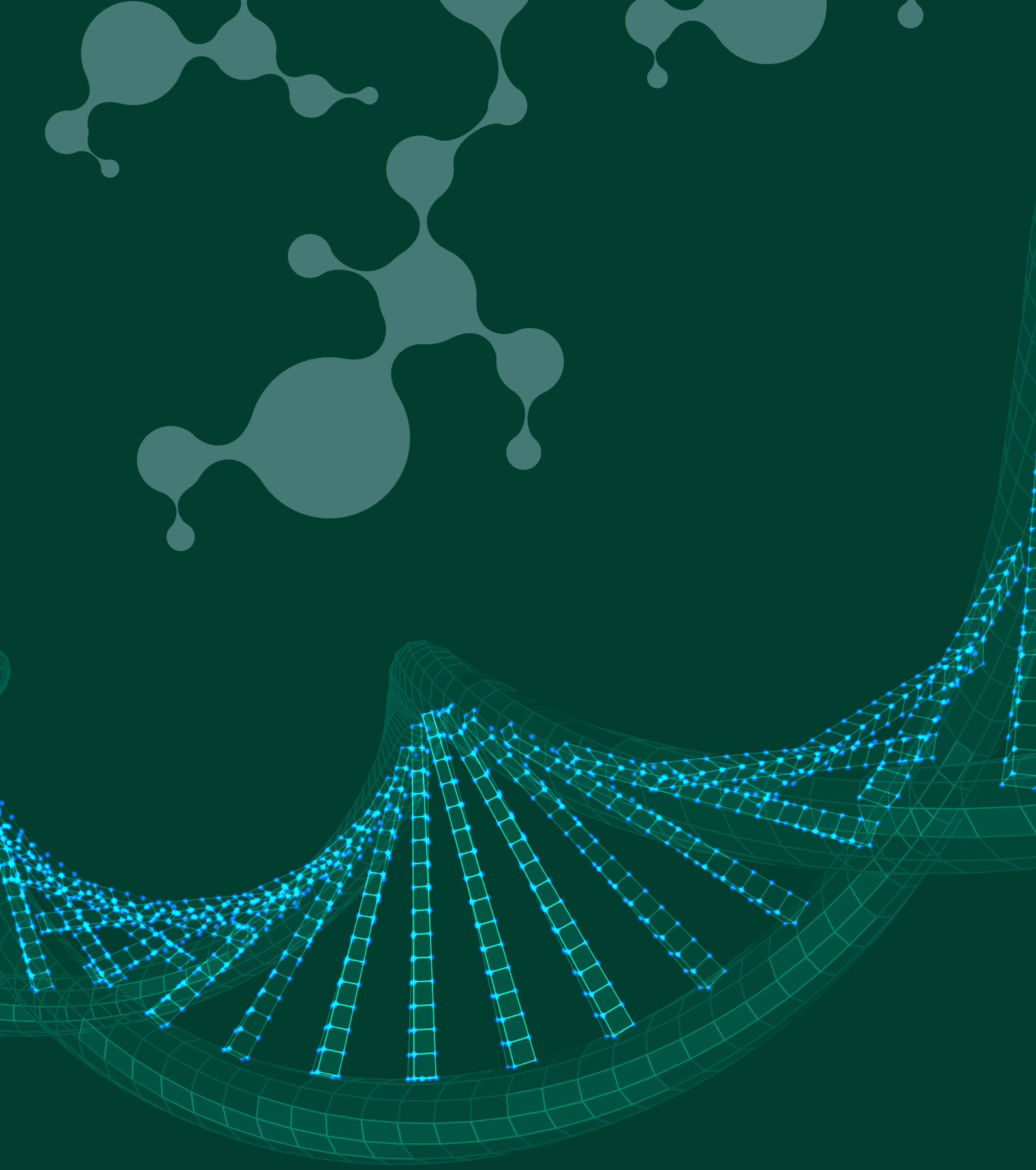
BLOOD BIOMARKERS FOR EARLY DETECTION OF PANCREATIC CANCER: OPPORTUNITIES AND CHALLENGES

Dr. Prof. Yu-Ting Chang
Professor
National Taiwan University; National Taiwan University Hospital
Department of Internal Medicine
Division of Gastroenterology/Hepatology

The accurate and timely detection of pancreatic ductal adenocarcinoma (PDAC) remains a significant challenge in the medical field. The use of blood-based biomarkers for the detection of cancer, such as microRNA, extracellular vesicles cell-free DNA/circulating tumor DNA, proteomics, and metabolomics, is a rapidly growing field with incredible potential. We have developed a unique diagnostic system that combines Probe Electrospray Ionization Mass Spectrometry (PESI-MS) and Machine Learning for the diagnosis of PDAC. In this study, PESI-MS analysis of 5 µl serum samples from 322 consecutive PDAC patients and 265 controls with a family history of PDAC was conducted, followed by machine learning algorithms to differentiate between control and cancer cases. A total of 587 serum samples were analyzed, revealing a sensitivity of 90.8% and specificity of 91.7% using the machine learning algorithm and PESI-MS profiles to identify PDAC. When combined with age and CA19-9 as predictors, the accuracy for detecting stage 1 or 2 PDAC was 92.9%, and for stage 3 or 4, it was 93%. The simplicity and accuracy of PESI-MS profiles, along with machine learning, provide a promising opportunity to detect PDAC at early stages, particularly in at-risk populations. In addition, we also investigated the potential of Thrombospondin-2 (TSP-2) as a diagnostic marker for PDAC in a large Taiwan cohort and explored its association with clinical outcomes. Serum TSP-2 levels were measured in 263 PDAC patients and 230 high-risk individuals (HRIs) using an enzyme-linked immunosorbent assay. Significantly higher serum TSP-2 levels were observed in PDAC patients (44.90 ± 40.70 ng/ml) compared to HRIs (17.52 ± 6.23 ng/ml). At a cutoff value of 29.8 ng/ml, TSP-2 exhibited 100% specificity, 55.9% sensitivity, 100% positive predictive value (PPV), and 66.5% negative predictive value (NPV) for discriminating PDAC patients from HRIs. Furthermore, combining TSP-2 (cutoff value of 29.8 ng/ml) and carbohydrate antigen 19-9 (CA19-9) (cutoff value of 62.0 U/ml) levels resulted in 98.7% specificity, 90.5% sensitivity, 98.8% PPV, and 90.1% NPV for discriminating PDAC patients from HRIs. The incorporation of TSP-2 along with CA19-9 in a combined biomarker panel holds promise for enhancing future PDAC screening efforts. The challenges and opportunities of blood biomarkers for the detection of PDAC will be explored with the goal of identifying possible collaboration projects between the Taiwanese and Lithuanian scientists.

More about the scientist

Professor Yu-Ting Chang graduated from the Department of Medicine at the National Taiwan University College of Medicine in 1996. He obtained his MS and PhD degrees from the Graduate Institute of Pathology and the Graduate Institute of Clinical Medicine at the College of Medicine of National Taiwan University in 2001 and 2009, respectively. Since 2002, he has been an attending physician in the Department of Internal Medicine at National Taiwan University Hospital and currently holds the position of Professor in the Department of Internal Medicine at National Taiwan University College of Medicine since 2020. Professor Chang specializes in the development of advanced therapeutic endoscopic techniques, including Endoscopic Retrograde Cholangiopancreatography (ERCP), Interventional Endoscopic Ultrasound (EUS), and Endoscopic submucosal resection (ESD), for gastrointestinal oncology and biliary-pancreatic diseases at National Taiwan University Hospital. Since 2002, Professor Chang's research has focused on the pathogenesis, early diagnosis, treatment, and prognostic biomarkers of pancreatic diseases, particularly pancreatic ductal adenocarcinoma (PDAC). Over the past two decades, Professor Chang and his team have established the largest pancreatic disease cohort and biobank in Taiwan and have published several papers related to the diagnostic and prognostic biomarkers of PDAC, including Thrombospondin-2 (TSP-2), circulating tumor cells/clusters (CTCs), and erzin in exosomes. He has also formed an international collaborative research team with Leicester General Hospital in the United Kingdom and the University of Yamanashi in Japan to utilize Probe Electrospray Ionization Mass Spectrometry (PESI-MS) and Machine Learning to diagnose PDAC. In addition to his research work, Professor Chang is also the program director of the training program for internal medicine at the College of Medicine, National Taiwan University.



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