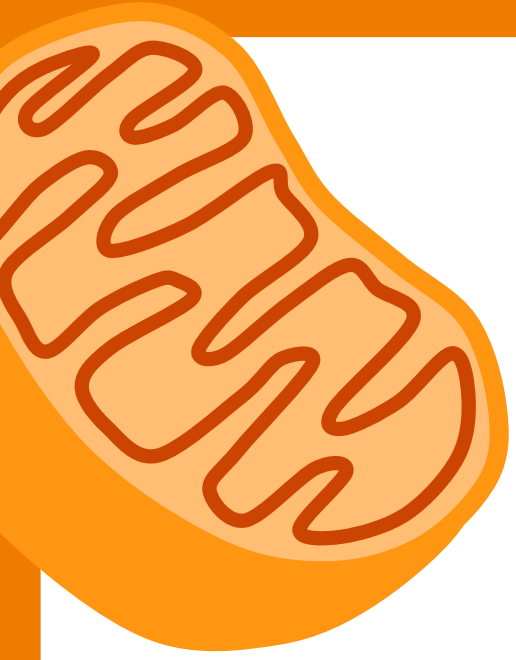

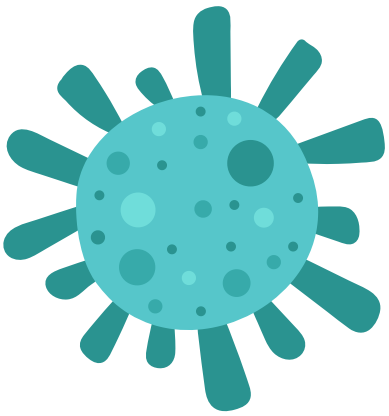

6TH NUS-CMU JOINT SYMPOSIUM

November 26-27, 2024

NUS, University Hall Auditorium

NUS National University of Singapore | Department of Physiology
Yong Loo Lin School of Medicine

CONTENTS

WELCOME NOTE

Dear Colleagues,

On behalf of the Department of Physiology, it is our pleasure to welcome you to the 6th National University of Singapore (NUS) -China Medical University (CMU) joint symposium. Over the years, the annual symposium between NUS and CMU has provided a platform to bring together experts in various fields including cancer biology, neuroscience, and ageing. This year, the symposium is focused on cancer biology. We are thrilled to have a fantastic group of thought leaders for meaningful discussions in the areas of Signal Transduction and Tumor Immunology, Cancer Epigenetics and Therapeutics, and Cancer Mechanisms and Interventions. We are confident that the exchanges will foster new partnerships and collaborations between the two universities.

We would like to express our gratitude to all our speakers, session chairs, and judges of poster presentations who have generously agreed to share their expertise and time with us.

A special thank you to Prof. Koh Dow Rhoon and Prof. Yang Liang-Yo for their staunch support in facilitating the annual NUS-CMU symposia. We are indebted to the Yong Loo Lin School of Medicine for providing generous support for this meeting.

Our sincere thanks to Crystal Heng, and the organizing committee members - Lim Hong Meng, Unis Yeo, Tiara Zuraini, and Lee Suk Yin who have worked tirelessly behind the scenes to help with logistics. Without their dedication and hard work, none of this would have been possible.

We look forward to engaging conversations, future collaborations and lasting connections that will emerge from this symposium and wish you all a productive and enriching experience.

Reshma Taneja
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Healthy Longevity, N2CR and CVMD Translational Research Programme,
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ORGANIZING COMMITTEE

CO-CHAIRS:

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DR. DERRICK ONG

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DR. SHIH-YIN TSAI

COMMITTEE MEMBERS

UNIS YEO YONGXIN

TIARA CAMELIA ZURAINI

LEE SUK YIN

LIM HONG MENG

SCIENTIFIC PROGRAMME

Day 1 (Tuesday, 26th November 2024)	
8:00 - 8:45am	Registration
8:45 - 8:55am	Opening Remarks Prof Chong Yap Seng, Dean, Yong Loo Lin School of Medicine, National University of Singapore Prof Mien-Chie Hung, President, China Medical University
Session 1: Signal Transduction and Tumor Immunology Chairs: Thai Tran and Stephen Chong	
8:55 - 9:40am	**KEYNOTE ADDRESS** **Mien-Chie Hung** **Marker-guided effective therapy (MGET)** **China Medical University**
9:40 - 10:00am	**Shazib Pervaiz** **Redox Perspective on Cancer Cell Fate Signaling** **Yong Loo Lin School of Medicine, National University of Singapore**
10:00 - 10:20am	**Shruti Bhatt** **Targeting Therapy Resistance in TP53 Inactivated Cancers** **Faculty of Science, National University of Singapore**
10:20 - 10:50am	**Tea Break**
10:50 - 11:10am	**Boon Cher Goh** **Targeting the immune microenvironment of EBV nasopharyngeal carcinoma** **Cancer Science Institute of Singapore**
11:10 - 11:30am	**Herbert Schwarz** **Coinhibition by CD137 - The lesser known side of a potent costimulatory molecule** **Yong Loo Lin School of Medicine, National University of Singapore**
11:30 - 11:50am	**Hung-Rong Yen** **Combinational Cancer Immunotherapy with Chinese Herbal Medicine for Pancreatic Cancer** **China Medical University**
11:50 - 12:10pm	**Shao-Chun Wang** **Evading Anti-Tumor Immune Surveillance Through Tyrosine Phosphorylation of Proliferating Cell Nuclear Antigen (PCNA)** **China Medical University**
12:10 - 1:40pm	**Lunch**

SCIENTIFIC PROGRAMME

Day 1 (Tuesday, 26th November 2024)	
Session 2: Cancer Epigenetics and Therapeutics **Chair: Celestial Yap**	
1:40 - 2:00pm	Giorgia Pastorin Red Design of PT(IV) Anticancer Complexes, Screening in 3D Spheroids and Delivery to Animal Cancer Models Faculty of Science, National University of Singapore
2:00 - 2:20pm	Wei-Chien Huang New Mechanism For Anti-Cancer Drug Discovery China Medical University
2:20 - 3:05pm	KEYNOTE ADDRESS Wee Joo Chng Superenhancers in Myeloma Cancer Science Institute of Singapore
3:05 - 4:05pm	Flash Talks
4:05 - 4:35pm	Tea Break
4:35 - 6:00pm	Discussion on Collaboration
7:00 - 9:00pm	Dinner (Invited guests only)
End of Day One	

SCIENTIFIC PROGRAMME

Day 2 (Wednesday, 27th November 2024)	
8:00 - 8:30am	Registration
Session 3: Cancer Mechanisms and Interventions Chairs: Tee Wee Wei and Ling Shuo-Chien	
8:30 - 9:15am	**KEYNOTE ADDRESS** **Ashok Venkitaraman** **Mechanisms driving early steps in cancer evolution** **Yong Loo Lin School of Medicine, National University of Singapore**
9:15 - 9:35am	**Derrick Ong** **Uncovering novel glioblastoma dependencies for mechanism-guided therapies** **Yong Loo Lin School of Medicine, National University of Singapore**
9:35 - 9:55am	**Lih-Wen Deng** **Therapy Resistance in Cervical Cancer and its Therapeutic Strategies** **Yong Loo Lin School of Medicine, National University of Singapore**
9:55 - 10:15am	**Karen Crasta** **Differential therapeutic benefit for breast cancer dictated by distinct extracellular vesicle-mediated inflammatory response** **Yong Loo Lin School of Medicine, National University of Singapore**
10:15 - 10:45am	**Tea Break**
10:45-11:05am	**Anthony Khong** **Stress Granule Assembly and Functions** **Yong Loo Lin School of Medicine, National University of Singapore**
11:05-11:25am	**Yuh-Pyng Sher** **Targeting Cancer Metastasis in Translational Medicine: A New View on ADAM9** **China Medical University**
11:25 - 11:45am	**Yi-Hung Chen** **Analgesic and Neuroprotective Effects of Electroacupuncture: Fundamental Insights** **China Medical University**
11:45 - 12:00pm	Closing Remarks by Prof Koh Dow Rhoon and Prof Yang Liang-Yo
12:00 - 1:30pm	**Lunch**
1:30 - 3:00pm	**Discussion for Collaboration**
5:00 - 6:00pm	**Sight-seeing** Botanic Gardens
6:00 - 8:00pm	**Dinner (Invited guests only)**
End of Day Two	

KEYNOTE SPEAKERS

Mien-Chie Hung

President, China Medical University

Biography:

Mien-Chie Hung, Ph.D. is the President for China Medical University in Taiwan. He was vice president for basic research, and held a Distinguished Endowed Chair of the Department of Molecular and Cellular Oncology at The University of Texas MD Anderson Cancer Center. He is a basic scientist with a keen translational vision and especially his recent research effort has significantly contributed to understanding the biology of cancer and to developing combinational cancer therapies to overcome resistance. He has published more than 650 peer-reviewed articles. His lifetime h-index reaches to 173 (Google Scholar) and 150 (Scopus), respectively. He is one of members of Selection Committee for Tang Prize in Biopharmaceutical Science category and is one of the founding Editorial Members for Cancer Cell (2002-2020), serves as Molecular Cell Advisory Board Member (2020-present); Cancer Research Senior Editor (2018-2021); American Journal for Cancer Research (AJCR) Editor-in-Chief (2015-2017; 2020-present); Cancer and Metastasis Reviews Editor (2018-present), Cancer Letters Senior Editor (2024-present), etc. Dr. Hung was appointed as an Academician of the Academia Sinica in Taiwan in 2002, elected as a Fellow in the Biological Sciences section of the American Association for the Advancement of Science in 2010, and later honored as a Fellow of The World Academy of Sciences (TWAS) for the Advancement of Science in Developing Countries in 2023. His research interests are focused on: 1) Elucidation of non-canonical signal pathways of Receptor Tyrosine Kinases and novel posttranslational modifications that play critical roles in tumor progression; 2) Identification of crosstalk signaling pathways to understand drug resistance mechanisms for targeted therapy then develop effective therapy to overcome drug resistance; 3) Development of effectively immunotherapy and study of resistant mechanisms of immunotherapy.

Title: Marker-guided effective therapy (Mget)

Cancer therapy has moved into a new era, including mechanism-driven marker-guided target therapy and immune therapy. Anti-PD-1/PD-L1 therapy is a promising immune therapy for multiple cancer types. Glycosylation of PD-L1 is required for its protein stability and interaction with PD-1 (Nature Comm 2016). Impressive therapeutic effect of developed glycosylation-specific PD-L1 mAb was observed through antibody-drug-conjugate approach (Cancer Cell 2018a & Cancer Res 2020). Through identifying potential targets, we developed marker-guided effective therapy (Mget) to enhance therapeutic efficacy and/or overcome drug resistance by combination therapy with immune checkpoint therapy, including metformin (Mol Cell 2018), c-MET inhibitors (Gastroenterology 2019); and targeting IL-6/JAK1 pathway (J Clin Invest 2019), Galectin-9 (Nature Comm 2021, IJBS 2023a), Tyro 3 (J Clin Invest 2021). Several PARP inhibitors have been approved to treat cancer patients with BRCA mutation and/or homologous recombination defective tumors, we also investigate the mechanisms inducing resistance to PARP inhibitors and develop marker-guided combination therapy to overcome the resistance. The goal is to use identified markers to stratify patients for the right combination therapy. These include reports on c-Met, ALK and GSDMC (Nature Medicine 2016; Nature Cancer 2022 & JCI 2024). This talk will also include our discoveries on novel therapy overcoming resistance to EGFR TKI in lung cancer (Cancer Cell 2018b , clinical trial, NCT06071013 is ongoing) and other caner types as well as a new methodology to retrieve antigen by protein de-glycosylaton that improves predictive ability of PD-L1 as a biomarker for immunotherapy. (Cancer Cell 2018b, Cancer Cell 2018c, Cancer Cell 2019, AJCR 2022a, Nature Reviews Clinical Oncology 2022, Nature, 2020, Nat. Cell Biol 2020; Mol Cell 2021, IJBS 2023a,b,c, Nature Comm 2024). We will also share with our recent unpublished data for markers-guided effective therapy using novel serum markers (ChiCTR2100054794, submitted). All efforts are focused on mechanism-driven marker-guided effective therapy in a hope to benefit cancer patients.

KEYNOTE SPEAKERS

Wee Joo Chng

Cancer Science institute of Singapore, NUS
Dept of Medicine, Yong Loo Lin School of Medicine, NUS
National University Cancer Institute, Singapore, NUHS

Biography:

Professor Wee Joo Chng is Vice President (Biomedical Sciences Research) at the National University of Singapore and Senior Principal Investigator of the Cancer Science Institute of Singapore. He is currently the Yong Loo Lin Professor in Medical Oncology at the Yong Loo Lin School of Medicine, the Group Director of Research at the National University Health System, and the inaugural Executive Director of the Singapore Translational Cancer Consortium. A hematologist by training, Professor Chng is an esteemed researcher in genomics, therapeutics and hematologic malignancies, with extensive experience in clinical practice, administration, and leadership. He has produced highly translational research, such as using global genomic techniques to better understand drug resistance and disease prognosis in hematological malignancies, which has resulted in more personalized treatment and improved patient outcomes. Professor Chng's impactful research has won him numerous national and global accolades, including the International Myeloma Foundation's Brian G.M. Durie Outstanding Achievement Award in 2020, making him the first in Asia to receive this honour, and the National Medical Research Council's National Outstanding Clinician Scientist Award in 2016.

Professor Chng has been a Senior Consultant at the National University Cancer Institute, Singapore for more than two decades. He has also served as Vice Dean of Research at the Yong Loo Lin School of Medicine (2022 – 2023), Director of the National University Cancer Institute, Singapore (2014– 2023), and Provost's Chair (2018 – 2022). He also serves on important national and international professional committees, including the American Association of Cancer Research, and was previously President of the Singapore Society of Hematology.

Professor Chng obtained his medical degree from the University of Leeds and completed his internal medicine residency and fellowship training in hematology in the United Kingdom and Singapore, respectively.

Title: Superenhancers in myeloma

Multiple myeloma is a hematological malignancy arising from immunoglobulin-secreting plasma cells. It remains poorly understood how chromatin rewiring of regulatory elements contributes to tumorigenesis and therapy resistance in myeloma. Super-enhancers (SEs) are large clusters of putative enhancers densely occupied by mediators and transcription-regulating proteins that evoke stronger transcriptional activation compared to typical enhancers. We generate a high-resolution contact map of myeloma-associated super-enhancers by integratingH3K27ac ChIP-seq and HiChIP from myeloma cell lines, patient-derived myeloma cells and normal plasma cells. Our comprehensive transcriptomic and phenomic analyses prioritize candidate genes with biological and clinical implications in myeloma.

KEYNOTE SPEAKERS

Ashok Venkitaraman

Director

Cancer Science Institute of Singapore

Biography:

Ashok Venkitaraman is a Distinguished Professor of Medicine at the National University of Singapore, the Director of the Cancer Science Institute of Singapore, and a Research Director at the Institute of Molecular & Cell Biology, A*STAR. He learnt and practiced medicine at the Christian Medical College, Vellore, India before his Ph.D. with Sir Marc Feldmann at University College London. After his postdoctoral work with Michael Neuberger, Ashok established his research group at the Medical Research Council (MRC) Laboratory of Molecular Biology, Cambridge, prior to his election as the inaugural holder of the Ursula Zoellner Professorship of Cancer Research at the University of Cambridge from 1998–2020. He was the Director of the MRC Cancer Unit in Cambridge from 2006–2019. Ashok's research has contributed fundamentally to our understanding of how human cancer is suppressed by genes that maintain the integrity of the genome. He is recognized for discovering the functions of the breast cancer gene, BRCA2, laying the scientific foundations for approaches to targeted therapy and cancer prevention. Ashok has also pioneered new technologies that enable the precise identification and validation of therapeutic targets, leading to the serial spin-out by Cambridge University of biotechnology firms like PhoreMost based on his research.

Ashok's work has been recognized by international awards, and appointments to the advisory boards of leading academic and commercial organizations. He was inducted as a fellow of the Academy of Medical Sciences, one of the UK's four national academies, in 2001, and as a member of EMBO in 2004.

Title: Mechanisms driving early steps in cancer evolution

Cancer risk is determined by interactions between genetic inheritance and environmental exposures. How these factors collude to promote early steps in cancer evolution is poorly understood at the molecular level. We have used cancer susceptibility in carriers of mutations affecting the breast cancer gene, BRCA2, as a powerful model system to address this problem. Here, I will discuss recent work from our laboratory that highlights a new molecular mechanism connecting alterations in energy metabolism with inactivation of the tumour suppressive functions of BRCA2. Our work suggests a model wherein derangements in energy metabolism caused by metabolic disorders, diet or oncogenic drivers suffice to initiate early steps in cancer evolution.

SPEAKERS

Shazib Pervaiz

Professor

Yong Loo Lin School of Medicine, National University of Singapore

Biography:

Shazib Pervaiz obtained his clinical degree (MBBS) from King Edward Medical College, Lahore, and his PhD from SMU, Dallas, TX, USA. He was a post-doctoral fellow in Pathology/Cancer Centre at Harvard Medical School/MGH, Boston, MA, from 1992-96. He joined NUS in 1996 where he holds a Professorship in the Yong Loo Lin School of Medicine. Over the years, he has held strategic leadership positions, such as Vice Dean Research and Graduate Education. He is a Theme Lead and member of the Executive Committee of NUS Centre for Cancer Research (N2CR) and an affiliate member of NCIS, NUHS, Singapore. Dr Pervaiz also held a joint Professorship at Duke-NUS GMS, Singapore (2007-2015) and is Adjunct Professor at University of Paris, France. His group is investigating the mechanisms of drug resistance in cancers with a specific focus on cellular redox metabolism. He has authored more than 170 papers and has a H-index of 56 (Google scholar). He was awarded NUS Outstanding Researcher Award in 2005 and has been a recipient of several teaching awards. He has been a speaker at several international venues and serves on editorial boards of several peer-reviewed journals. He was elected to the European Cell Death Organization Academy in 2013 and serves on the Board of International Cell Death Society. Dr Pervaiz has supervised doctoral theses of more than 40 graduate students and trained an equal number of postdoctoral fellows. He is also a certified Life Coach with a strong belief in the power of introspective transformation.

Title: Redox Perspective on Cancer Cell Fate Signaling

Intracellular redox state is a critical determinant of cancer cell fate. While an overwhelming increase in reactive oxygen and/or nitrogen species (ROS/RNS) results in cell death and tissue damage, there is preponderance of evidence to implicate mild 'pro-oxidant' milieu in cell proliferation and survival. To that end, our work over the years has unraveled signaling networks and biological processes influenced by aberrant redox environment of cancer cells. Using a variety of model systems, we provide evidence that an increase in intracellular superoxide as well as the ratio of superoxide to hydrogen peroxide endows cancer cells with a survival advantage. The differential ROS signaling has been linked to inactivation of the putative tumor suppressor phosphatase PP2A, which regulates the phosphorylation of key oncogenic proteins such as c-myc, Bcl-2 and NF-kB as well as stabilizes tumor suppressors such as p53. On the flip side of it, our recent findings highlight a novel approach to leverage on the aberrant redox environment of cancer cells for therapeutic targeting. In this regard, drug-induced hyperactivation of KRAS is shown to selectively trigger oxidative stress-mediated execution of mutant KRAS driven cancers. These observations underscore the critical role that tumor microenvironment plays in the dichotomy of redox signaling in cancer cell fate decisions, which has potential translational relevance from the standpoint of developing novel therapeutics.

SPEAKERS

Shruti Bhatt

Assistant Professor

Faculty of Science, National University of Singapore

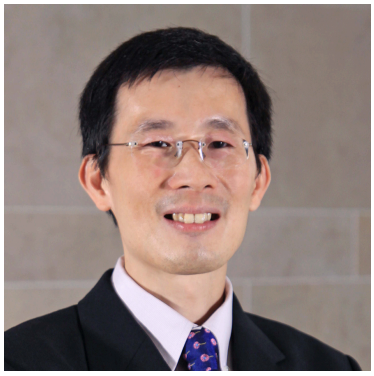
Biography:

Shruti Bhatt is an Assistant Professor at the National University of Singapore in the Department of Pharmacy. Her research lab focuses on understanding the mechanism of resistance to targeted therapy and developing new therapeutic strategies for relapsed leukemia using functional and genomic approaches. Dr. Bhatt completed postdoctoral training in the laboratory of Dr. Anthony Letai at Dana-Farber where she worked on personalizing leukemia therapy by exploiting mitochondrial pathway of apoptosis. Dr. Bhatt obtained PhD in Pharmacology from University of Miami where she trained under Dr. Izidore Lossos and developed novel antibobdy-cytokine fusion protein to target lymphoid tumors. Dr. Bhatt has received number of fellowships/awards including, LLS CDP Fellow Award, ASH Global Research Award, early career AACR Nextgen Stars Award and EMBO Global Investigator Award.

Title: Targeting therapy resistance in TP53 inactivated cancers

Despite extensive research on the TP53 network, the mechanisms underlying therapy resistance in TP53-inactivated cancers remain poorly understood. We employed a multiomics approach, integrating whole-genome CRISPR screening, transcriptomics, proteomics, and high-throughput drug screening in isogenic acute myeloid leukemia (AML) models to elucidate these mechanisms. Our findings reveal that TP53-inactivated tumors retain the capacity for mitochondrial outer membrane permeabilization (MOMP) despite downregulation of p53-induced pro-apoptotic targets. However, a conserved phenomenon across TP53-inactivated AML and multiple cancers is the failure to activate executioner caspases in response to therapy, leading to apoptosis evasion. We identified BIRC5 (survivin) as a functional vulnerability in TP53-inactivated tumors. TP53-inactivated AML primary tumors and 19 out of 25 TCGA cancer types failed to negatively regulate BIRC5. Inhibitors of survivin and inhibitor of apoptosis proteins (IAPs) demonstrated high efficacy in overcoming resistance to standard-of-care therapy in multiple TP53-inactivated cancers. In vivo studies using survivin and IAP inhibitors showed superior leukemia blast inhibition in TP53-inactivated xenografts. This discovery of caspase blockade and BIRC5 dependency as drivers of apoptosis evasion opens new therapeutic avenues for highly morbid TP53-inactivated cancers.

SPEAKERS



Boon Cher Goh

Deputy Director

Cancer Science Institute of Singapore

Biography:

Dr Boon Cher Goh is a clinician scientist with interest in development of novel therapeutics for cancer, particularly in head and neck and lung cancer. He leads the phase 1 clinical trial team at the National University Cancer Institute, a well-established team conducting novel first in human and combination agent studies of industry and investigator hypothesis testing trials. At the Singapore Translational Cancer Consortium, a government national cancer research initiative, he co-leads the clinical trials strategic platform. Dr Goh is also senior PI at the Cancer Science Institute, where his laboratory is focused on discovering novel disease mechanisms especially in head and neck cancer including endemic EBV associated nasopharyngeal carcinoma through functional genomics and validation on patient derived models.

Title: Targeting the immune microenvironment of EBV nasopharyngeal carcinoma

Nasopharyngeal carcinoma is an EBV related cancer that is endemic in East Asian countries and 80% of patients present with advanced stages and are at risk of relapse. Due to its chemosensitivity, metastatic disease is treated with platinum-gemcitabine based chemotherapy, with a high objective response rate of ORR of 64% and progression free survival (PFS) of 7 months. Second-line treatment after platinum chemotherapy has a guarded prognosis with median PFS ranging from 4-6 months. Eighty-five percent of these patients will succumb within a year and virtually all die within 3 years. As EBV-related NPC is characterised by a prominent inflammatory infiltrate associated with high programmed death ligand 1 (PD-L1) expression, there has been immense interest in studying the effect of immunotherapy on NPC in recent years. Single cell ribonucleic acid (RNA) sequencing revealed predominance of T cell exhausted states with subpopulations of immunoregulatory cells in the tumour microenvironment. However, response rate to anti-PD1 monotherapy has been met with surprisingly modest objective tumour response for undefined reasons. Indeed, in platinum failure patients, pembrolizumab monotherapy was not superior to single agent chemotherapy. Incorporation of anti-PD1 with chemotherapy in first line has had more success though the mechanism of this combination is unclear. Vascular endothelial growth factor (VEGF) is upregulated in NPC tumour microenvironment (TME) and has the potential to impede immune cell trafficking, promote immune tolerance by dampening the immune response through immature dendritic cell maturation, increased T regulatory cells and MDSCs and anti-inflammatory macrophages. Our previous work has shown that a week of anti-VEGF treatment leads to increased CD4 and CD8 T cell infiltration into the NPC TME, whether this improves anti-PD1 therapy is unclear. We conducted a phase II open-label randomised study comparing pembrolizumab with the combination of pembrolizumab and bevacizumab in patients with NPC who had progressed after platinum-based chemotherapy. To gain insights to the mechanism of immune activation, we analysed serially sampled tumour and blood for evidence of immune activation in response to VEGF and anti-PD1 therapy, showing that the combination treatment has a profound effect in reprogramming the TME towards restoration of immune rejection of NPC and represents a therapeutic advancement.

SPEAKERS

Herbert Schwarz

Deputy Head of Department

Yong Loo Lin School of Medicine, National University of Singapore

Biography:

Herbert Schwarz is an Associate Professor at the Dept of Physiology and the ImmunologyTranslational Research Programme at the National University of Singapore.

Dr. Schwarz received his Ph.D. in Genetics at the University of Würzburg, Germany, in 1989. After a postdoc at the ScrippsResearch Institute in San Diego, CA, he joined the University of California, San Diego, in 1991,where he cloned the human gene for CD137. In 1994 he moved to the University of Regensburg,Germany, where his group discovered and characterized many functions and aspects of the CD137biology. Between 1999 and 2004, Dr. Schwarz headed the Cellular Immunology Dept. at Xenova,Inc., in Cambridge, UK, and the Preclinical Research Dept. at Pieris Proteolab in Freising, Germany.During his time in Biotech industry Dr. Schwarz was responsible for the preclinical research anddevelopment of several drug candidates for immunotherapy of cancer and autoimmune disease. Dr.Schwarz joined NUS in 2004, where his group is exploring the role of CD137 in anti-tumor immuneresponses and aims to use this knowledge in the development of novel immunotherapy approaches.

Title: Coinhibition by CD137 - The lesser known side of a potent costimulatory molecule

CD137 is a powerful costimulatory molecule on T cells, and crosslinking of CD137 enables T cells to reject tumors. The ligand for CD137, CD137L, is expressed by antigen presenting cells (APC), and APC use the CD137-CD137L system to costimulate T cells. The CD137 receptor / ligand system has an inbuilt negative feed-back mechanism to prevent overstimulation of the immune response and subsequent autoimmune damage. We identified this mechanism which consists of the trogocytic transfer of CD137 from activated T cells to APC, and the subsequent downregulation of the immunostimulatory CD137L.

This physiological feed-back mechanism is also employed by regulatory T cells (Treg) to keep T cell responses in check. It is hijacked by tumors as it facilitates their escape from immune surveillance. CD137 is especially highly expressed by Tregs that have infiltrated tumors, and CD137 was found to be that marker that most significantly distinguishes peripheral from intratumoral Treg. CD137+ Treg were identified in all solid cancers tested, and a high frequency of CD137+ Treg correlates with a poor prognosis.

Further, in Hodgkin Lymphoma, nasopharyngeal carcinoma and rhabdomyosarcoma even malignant cells express CD137 as it helps them to fend off an anti-cancer immune response.

However, CD137 expression may be a cancer's Achilles heel, as it can be targeted by immunotherapy. We developed a chimeric antigen receptor against CD137, and antibodies that can induce antibody-dependent, cell-mediated cytotoxicity in CD137-expressing cancer cells and Treg. One of these antibodies crossreacts with murine CD137, thus allowing to demonstrate proof of principle in murine tumor models.

SPEAKERS

Hung-Rong Yen

Professor and Dean
China Medical University

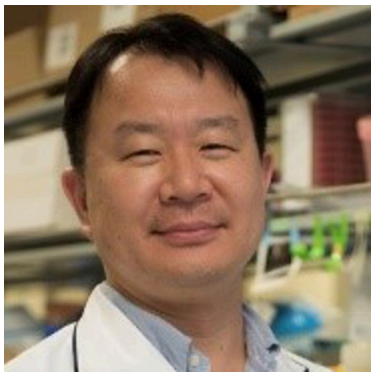
Biography:

Professor Hung-Rong Yen is a physician-scientist. He earned his M.D. degree with a dual major in Western and Chinese medicine from China Medical University and subsequently completed clinical training in both Western medicine and Chinese medicine at Chang Gung Memorial Hospital. Additionally, he obtained his Ph.D. from Chang Gung University and completed a three-year research fellowship in immunology at Johns Hopkins University, USA. Professor Yen's comprehensive academic and research background spans multiple biomedical fields. As a physician-scientist with dual clinical training in both Western and Chinese medicine, he is a prominent advocate for integrating Chinese medicine into conventional healthcare. He is dedicated to mentoring the next generation of physicians and fostering collaboration across diverse medical disciplines. His integrative clinical practice teams have been honored with two "Symbol of National Quality" (SNQ) Awards in Taiwan, and his research on Taiwan's native herbal medicine has earned a "National Innovation Award." He was awarded the "Best Doctor of the Year 2023 in Taiwan" in the Chinese medicine specialty. He is ranked among the "World's Top 2% Scientists", including both "Lifetime Science Influence Rankings" and "Single-Year Science Impact Rankings," with recognition extending through consecutive years. Furthermore, he is a pioneer in innovative teaching methods in Chinese medicine education, incorporating OSCE, MOOCs, VR applications, and EMI courses. His English-taught TCM course "Traditional Chinese Medicine: from Basic Concepts to Clinical Application" was delivered to medical students in Yong Loo Lin School of Medicine at the National University of Singapore in 2021-2023. In 2024, he was invited to deliver a guest lecture for the General Education module "Chinese Medicine: Theory and Practice" (approximately 600 NUS students registered this course) by the Department of Chinese Studies, National University of Singapore.

Title: Combinational Cancer Immunotherapy with Chinese Herbal Medicine for Pancreatic Cancer

Metabolic reprograming of cytotoxic effectors by tumor microenvironment (TME) is one of the key mechanisms by which TME impairs the success of cancer immunotherapy. Therapeutic strategies that mitigate the immunosuppressive TME and selectively enhance bioenergetic fitness of cytotoxic effectors may enhance the benefits of immunotherapy, particularly in TME-abundant cancers. IL-17 is a key TME cytokine in a feed-forward loop promoting the immunosuppressive milieu and cancer progression. Mitochondria is a key metabolic regulator of T cell metabolic fitness. Therefore, we hypothesized that targeting IL-17 and mitochondrial metabolism by Chinese herbal medicine could enhance antitumor immune response and directly inhibit pancreatic cancer growth. Our work shows that regulating bioenergetic metabolism and mTOR signaling and through regulation of T-bet and IFN-gamma induction augments cytotoxic T cell responses in pancreas cancer. Furthermore, combined metabolic reprogramming and IL-17 inhibition induces synergistic anti-cancer immunotherapeutic effects and suppresses subsequent tumorigenesis in tumor-bearing mice, mechanisms required for the success of immunotherapy in the treatment of pancreatic cancer.

SPEAKERS



Shao-Chun Wang

Vice Dean
China Medical University

Biography:

Dr. Shao-Chun Wang completed his undergraduate studies in pharmacy at Taipei Medical University. He then earned his PhD in Genetics and Cell Biology from the University of Minnesota, Twin Cities, followed by post-doctoral research at the MD Anderson Cancer Center. In 2007, Dr. Wang joined the University of Cincinnati's Department of Cancer Biology as a faculty member, a position he continues to hold. In 2016, he joined China Medical University in Taiwan, where he played a key role in leading the Center for Molecular Medicine of the CMU hospital. In 2019, Dr. Wang was appointed director of the newly established Research Center for Cancer Biology at the university. Dr. Wang's research focuses on the mechanisms that regulate the interaction between cancer cells and the tumor immune microenvironment, and their functional contributions to tumor progression, therapeutic response, and metastasis.

Title: Evading anti-tumor immune surveillance through tyrosine phosphorylation of proliferating cell nuclear antigen (PCNA)

Proliferating cancer cells often experience replication stress, producing aberrant cytosolic DNA and triggering anti-tumor immunity. This abnormal DNA metabolism, evolving through deregulated growth, is increasingly recognized as a key mechanism linking the immune microenvironment and tumor tissue, influencing tumor progression. However, the mechanisms involved remain largely unclear. Proliferating cell nuclear antigen (PCNA) is an indispensable component of the DNA replication machinery, coordinating DNA replication and repair through differential post-translational modifications. In cancer cells, phosphorylation at tyrosine 211 of PCNA (pY211-PCNA) is crucial for active proliferation. Using knock-in mouse models where tyrosine 211 is replaced with phenylalanine, thereby lacking this specific phosphorylation, we demonstrate that inhibiting pY211 disrupts replication fork processivity, triggering single-stranded DNA (ssDNA) production by the MRE11 nuclease and subsequently activating the cGAS-STING pathway, which leads to an anti-tumor immune response by natural killer (NK) cells. In breast cancer patients, cytosolic ssDNA levels inversely correlate with pY211-PCNA expression, which is associated with poor overall survival. We further show that pY211-PCNA regulates site-specific post-translational modifications of MRE11, promoting its endonuclease activity and causally ssDNA generation. This induces type I interferon-activated cytotoxicity by NK cells, preventing distant metastasis. Mechanistically, Y211 phosphorylation of PCNA determines the recruitment of MRE11 modifiers, tuning its nucleolytic modes and ssDNA production. Using syngeneic mouse models and patient-autologous tumor organoid models, we demonstrate that targeting this mechanism enhances NK cell-mediated cytotoxic killing and tumor suppression. Our studies reveal the potential to develop therapies leveraging genomic instability and immune activation to target malignant tumors.

SPEAKERS

Giorgia Pastorin

Professor and Head of Department
Faculty of Science, National University of Singapore

Biography:

Giorgia Pastorin received her MSc degree in Pharmaceutical Chemistry and Technology in 2000 and her Ph.D. in Medicinal Chemistry in 2004 from the University of Trieste (Italy). She spent two years of her postDoc at the CNRS in Strasbourg (France), where she specialized in drug delivery.
She joined the National University of Singapore (NUS) in June 2006, as Assistant Professor in the Department of Pharmacy-Faculty of Science. She was promoted to Associate Professor in 2011, Assistant Head in 2014, Deputy Head in 2016 and Full Professor in 2024; she is currently Head of the Department of Pharmacy & Pharmaceutical Sciences at NUS.
Her research interest is focused on drug delivery, with the purpose of enhancing the pharmacological effects of bioactive agents (such as Pt-based anticancer complexes) while minimizing undesirable side effects. Recently, her BioNanoTechnology (BNT) group developed cell-derived nanovesicles (CDNs) and biohybrids as novel biocompatible Extracellular Vesicle mimetics for targeted drug delivery. Her approach of using unconventional yet efficacious cell-derived nanocarriers has become her signature program, resulting in new invention disclosures, industry engagements and even an international BioDrone award in 2021. She is the sole and co-Editor, respectively, of two books related to drug delivery and author in more than 160 articles in internationally peer-reviewed journals. For the work performed by her BNT group in NUS, she received the Young Scientist Award (2015) in NUS and she has been invited at prestigious international conferences as plenary or keynote speaker. So far, she has supervised about 30 PhD & Master students.

Title: Design of PT(IV) Anticancer Complexes, Screening in 3D Spheroids and Delivery To Animal Cancer Models

The discovery of cisplatin as a Platinum (Pt)-based anti-cancer drug in 1965 was an important milestone. Nowadays, cisplatin and its analogues, all acting at the nuclear DNA as their main biological target, are still used in more than 40% of all chemotherapy treatments. However, these drugs have toxic side effects (e.g. kidney dysfunction).
Hence, we have conceived novel dual-targeting platforms to ensure strategic delivery of dual-action Pt(IV) prodrugs: the first targeting was established by nanoencapsulation of Pt complexes to attain high accumulation at the tumor site. To achieve that, we developed a nano-biohybrid system called nano-Cell Vesicle Technology Systems (nCVTs), obtained through the fusion of cell-derived components with conventional synthetic materials. After the release of the Pt prodrug inside cancer cells, a second stage of targeting directed the Pt prodrugs to the mitochondria.
A spatial analysis was also performed to rationalize drug behavior and efficacy in a 3D tumor model: after 24 and 72h, spheroids were evaluated for changes in viability, expression of proliferation marker ki67, mitochondrial membrane potential and platinum accumulation. Images of fluorescently labelled spheroids enabled the discovery that one Pt(IV) complex uniquely induced permanent mitochondrial damage in spheroids after 24h. This extensive mitochondrial damage was corroborated through real-time observation of a rapid and increased intracellular platinum accumulation.
The Pt complexes showed excellent activity, characterized by low micromolar cytotoxicity and tumor remission in vivo, accompanied by reduced kidney toxicity and lack of peripheral neuropathy. One of them has shown the ability to be used as the first-in-kind oral Pt drug. Taken together, these research findings provide insights into the potential of nanomedicine to reach the diseased area, protect the incorporated bioactive molecules from premature deactivation and enhance delivery of Pt(IV) drugs at the mitochondria while decreasing their side effects.

SPEAKERS

Wei-Chien Huang

Professor

China Medical University

Biography:

Dr. Wei-Chien Huang completed his Master's studies in pharmacology at the National Cheng-Kung University (NCKU) in Tainan, Taiwan. In 2003, he earned his PhD in Pharmacology from the National Taiwan University (NTU), Taipei, Taiwan. He then completed his post-doctoral training at NTU in 2005 and the MD Anderson Cancer Center in Houston, Texas, in 2007. In 2008, Dr. Huang joined the China Medical University and Hospital as a faculty member, a position he continues to hold. During 2017-2022, Dr. Huang was appointed as the associate dean of the Research and Development Office at the university. Starting from this August, he was appointed as the director of the Program for Cancer Biology and Drug Discovery, which is a joint graduate program between CMU and Academia Sinica. Dr. Huang's research focuses on the mechanisms underlying tumorigenesis and acquired drug resistance, with the goal of developing new anti-cancer strategies.

Title: New mechanisms for anti-cancer drug discovery

HER2 plays an oncogenic role in a variety of cancers, including breast and gastric cancers. Through its tyrosine kinase activity, HER2 triggers multiple downstream survival and growth signals for tumor progression. Although HER2-targeted therapies, including monoclonal antibodies and tyrosine kinase inhibitors (TKIs), have been approved and widely used for these diseases, insensitivity, acquired resistance, and brain metastasis remain the unsolved challenges. Therefore, the development of a new therapeutic strategy by deciphering the mystery of HER2 is an urgent need for advanced HER2-positive cancer patients. In this study, we discovered a novel GTP-dependent serine kinase activity of HER2 for serine auto-phosphorylations (HER2 pSer), which is independent of tyrosine autophosphorylations. HER2 pSer, which are enhanced rather than inhibited by current HER2-targeted therapies, mediates cancer stemness and are associated with distant metastasis and poor survival rate. Through the virtual screening with 260,000 compounds, two direct HER2-binding compounds were identified to show promising inhibitory effects on HER2 pSer and resistance to HER2 TKIs. Our study provides new molecular insights into dual-specificity kinase (DSK) activity of HER2 for the development of new HER2-targeted therapeutic strategies.

SPEAKERS

Derrick Ong

Assistant Professor

Yong Loo Lin School of Medicine, National University of Singapore

Biography:

Derrick is the President's Assistant Professor at the Department of Physiology, National University of Singapore (NUS). He obtained his Bachelor in Science (First class Honors) and Masters in Biology at NUS, and PhD (Chemical Biology) at The Scripps Research Institute (TSRI), USA, where he trained under Dr Jeffery Kelly, a pioneer in the field of proteostasis. For his postdoctoral training, Derrick was mentored by Dr Ronald DePinho, a world expert in aging and cancer, first at Dana Farber Cancer Institute/ Harvard Medical School, and then at the University of Texas MD Anderson Cancer Center, USA His research is focused on identifying novel mechanisms of proliferation/ self-renewal of cancerous and normal brain stem cells. Derrick has also received several awards, including the National Research Foundation Fellowship, President's Assistant Professorship, Early Career Research Award, and the Yong Loo Lin School of Medicine Research Excellence Award.

Title: Uncovering novel glioblastoma dependencies for mechanism-guided therapies

Glioblastoma (GBM) is the most common and malignant adult brain tumor with an abysmal patient prognosis. The current standard of care for GBM remains to be aggressive surgery followed by radiotherapy, in combination with adjuvant temozolomide treatment. Tumor recurrence is almost inevitable due to the presence of glioma stem cells (GSCs), which exhibit stem cell-like traits, robust proliferation, invasiveness, therapy resistance and extensive cellular plasticity. We employ patient-derived GSCs as an experimental model to uncover new GBM dependencies that contribute to GBM clinical hallmarks. In this talk, I will outline our efforts towards a better molecular understanding of GBM pathogenesis by employing multi-dimensional analyses, and demonstrate how some of our findings may be translated into actionable clinical modalities. The long-term goal of our research is to develop biomarkers for patient stratification so as to aid precision medicine in GBM treatment.

SPEAKERS

Lih-Wen Deng

Associate Professor

Yong Loo Lin School of Medicine, National University of Singapore

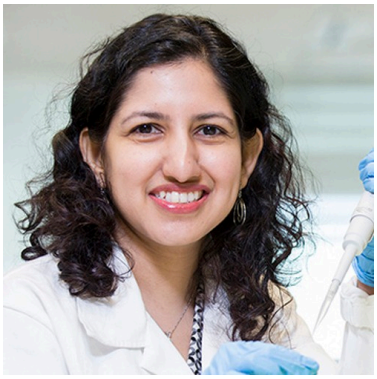
Biography:

Dr. Lih-Wen Deng is an Associate Professor in the Department of Biochemistry at the National University of Singapore (NUS). She received her Ph.D. from the University of Cambridge and completed her postdoctoral studies at Harvard University. Her research focuses on the molecular mechanisms of cancer development, particularly in therapy resistance and metastasis. Her recent work includes identifying cancer-testis antigens regulating chromatin dynamics in radioresistance and exploring cysteine metabolism in ovarian cancer. She collaborates with clinicians to develop prognostic markers and therapeutic strategies. She is also an affiliated member of NUS Center for Cancer Research and the National Cancer Institute Singapore.

Title: Therapy Resistance in Cervical Cancer and its Therapeutic Strategies

Cervical cancer results in approximately 340,000 deaths annually worldwide, with a significant portion developing resistance to standard cisplatin chemotherapy and radiotherapy (CCRT). In this talk, I will explore recent findings on cancer/testis G antigens (GAGE), highlighting its role as a predictor and mediator of radiotherapy resistance via chromatin dynamics regulation. We will also discuss a miRNA panel, developed in collaboration with NUS ncRNA Core, that predicts recurrence risk. Finally, new data on repurposing an FDA-approved drug for CCRT-resistant cancers will be presented, with a focus on patient stratification and personalized treatment strategies.

SPEAKERS



Karen Crasta

Research Assistant Professor

Yong Loo Lin School of Medicine, National University of Singapore

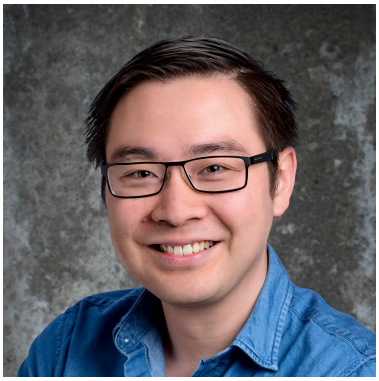
Biography:

Karen Crasta is an Assistant Professor at the National University of Singapore (NUS), Department of Physiology and Centre for Healthy Longevity where she leads the Genome Instability and Stress Response Laboratory. After BSc Honours at NUS, Karen completed her PhD at A*STAR Singapore in the lab of Prof. Uttam Surana where she uncovered fundamental mechanistic regulation underlying centrosome separation and mitotic spindle formation using budding yeast as a model system. Wanting to further her interests in the role of chromosome missegregation underlying cancers, she undertook postdoctoral training with Prof. David Pellman at the Dana-Farber Cancer Institute, Harvard Medical School where her work uncovered a mechanistic link between mitotic errors and chromosomal breaks via micronuclei. Following short stints upon her return to Singapore at A*STAR and LKCMedicine, she set up her research group at her alma mater NUS. Together with her team, Karen seeks to understand the impact of genome instability-related stress response and adaptation in cancer progression and therapeutic resistance, while investigating the translational potential of targeting the biological mechanisms of ageing. Karen is a recipient of the Singapore National Research Foundation (NRF) Fellowship, the A*STAR International Fellowship (AIF) and the HHMI Research Associate Fellowship (USA). She is also Deputy Director, Academic Outreach at NUS Dean's Office. Being a strong advocate for diversity, she has served as Executive Council Member on the NUHS Women in Science and Healthcare (WISH) Committee and is a Career Mentor under SINDA's "Let Her Shine" program.

Title: Differential therapeutic benefit for breast cancer dictated by distinct extracellular vesicle-mediated inflammatory response.

Triple-negative breast cancers, associated with poor prognosis and high tumour recurrence, are often-treated with taxanes in first-line treatment regimens. However, acquired disease resistance often sets in, hampering clinical efficacy. Senescent cells represent a population of residual disease that is highly secretory and drives cancer relapse. Although it is known that therapy-induced senescence can contribute to therapy resistance and cancer relapse via its secretome, the underlying cellular and molecular mechanisms are not fully understood. In this talk, I will discuss a recent study which uncovered an unexpected role for small extracellular vesicles within the senescent tumour cell-derived secretome where they confer critical impact as discrete entities which mediate distinct anti-tumourigenic properties and inflammatory response.

SPEAKERS



Anthony Khong

Assistant Professor

Yong Loo Lin School of Medicine, National University of Singapore

Biography:

Dr. Anthony Khong is an Assistant Professor in the Department of Physiology and the Cancer Science Institute in the National University of Singapore. He received his Bachelor of Science and Ph.D. from the University of British Columbia. Before joining the institute, Dr. Khong completed his postdoctoral fellowship at the University of Colorado Boulder, where he worked until 2023.

Dr. Khong specializes in RNA biology and the study of biomolecular condensates. His collaborative work in the Parker Lab has significantly advanced our understanding of stress granules, RNA-protein condensates that form in response to cellular stress. Through his work in describing stress granules transcriptome, Dr. Khong discovered that stress granules arise from non-specific RNA aggregation. This insight has not only reshaped the scientific understanding of stress granule assembly but also provided new perspectives on the formation and function of other RNA-protein condensates. Building on this work, Dr. Khong is now focused on dissecting the role of stress granules in cancer processes.

Title: Stress Granule Assembly and Functions

Tumors face a myriad of stressors, both intrinsic and extrinsic, stemming from genome instability and the tumor microenvironment, leading to detrimental conditions such as oxidation and proteotoxic stress. In response, post-transcriptional cellular mechanisms play a crucial role in addressing these challenges. Among these mechanisms, the integrated stress response pathway swiftly reduces global translation while selectively promoting the translation of genes vital for survival. Additionally, this pathway triggers the formation of stress granules, cytosolic biomolecular condensates believed to play a role in adaptive cellular responses and implicated in cancer biology. However, the exact role of stress granules in fostering adaptive responses during stress remains elusive.

Today, I will present a framework that sheds light on the role of stress granules in promoting adaptive responses during cellular stresses. This insight stems from my postdoctoral studies in Roy Parker's laboratory at the University of Colorado Boulder, where we focused on unraveling the nature of stress granules as RNA aggregates, and ongoing collaborations with Yue Wan's laboratory at A*STAR in mapping RNA structures within stress granules. This molecular understanding of stress granule assembly and dynamics enhances our comprehension of current research on stress granules, elucidating their involvement in virus infections, RNA quality control, and cancer biology.

SPEAKERS

Yuh-Pyng Sher

Professor

China Medical University

Biography:

Dr. Sher earned her M.S. in Microbiology and Immunology at National Taiwan University and received advanced training at the Institute of Biomedical Sciences (IBMS), Academia Sinica. She pursued her Ph.D. under the mentorship of Drs. Konan Peck, Chia-Li Yu, and Pan-Chyr Yang at National Taiwan University. Following her Ph.D., Dr. Sher was awarded the 2007 NHRI Postdoctoral Fellowship and began postdoctoral training under the mentorship of Academician Dr. Mien-Chie Hung at China Medical University Hospital. She subsequently advanced her academic career at China Medical University, where she is currently a Professor.

Dr. Sher's research primarily focuses on elucidating the molecular mechanisms driving lung cancer metastasis to the brain and identifying biomarkers for early detection. Additionally, her lab investigates the mechanisms of metastasis in other cancers prevalent in Taiwan with limited treatment options, such as esophageal and pancreatic cancers. These studies integrate biochemical techniques, clinical research, and experimental mouse models to explore cancer metastasis.

Her laboratory also focuses on translational medicine, aiming to develop innovative cancer therapies for clinical use. Dr. Sher's team has developed small molecule ADAM9 inhibitors that have demonstrated the ability to inhibit the growth of lung, breast, pancreatic, and esophageal cancer cells, prevent metastasis, and pass safety assessments. This patented technology has received international recognition, with patent filings in the US, EU, and China. Looking forward, her research is focused on developing combination therapies to enhance treatment efficacy and speed up clinical applications.

Title: Targeting cancer metastasis in translational medicine: A New View on ADAM9

Metastasis significantly contributes to elevated mortality rates across diverse cancer types, underscoring the pressing demand for targeted metastasis suppression therapies. Our research has illuminated the pivotal role of the membrane surface protein ADAM9 in amplifying the plasminogen activator-based pathway within brain-metastatic lung cancer cells. This pathway, critical for clot breakdown, was found to be potentiated by ADAM9, as substantiated by animal models and clinical specimens (Cancer Research, 2014). An unexpected revelation emerged from our investigation: ADAM9's membrane presence enables its translocation into the nucleus, exerting influence over chromatin, and orchestrating the transcription of angiogenesis-related genes. In this nuclear role, ADAM9 acts as a transcriptional repressor, culminating in sustained low levels of PAI-1 and inhibition of anti-angiogenic activity, thereby fostering angiogenesis (International Journal of Biological Sciences, 2021). Furthermore, our discernment led us to identify four genes (ADAM9, MTHFD2, RRM2, and SLC2A1) endowed with potential as theranostic biomarkers. These biomarkers hold promise for stratifying high-risk patients prone to relapse/metastasis in early-stage LUAD (Theranostics, 2021). Pancreatic cancer presents a formidable challenge in therapeutic intervention due to the enduring resistance posed by KRAS signaling over the past three decades. The inherent diversity of KRAS mutations and the coexistence of multiple KRAS mutants within pancreatic tumors render targeting a single mutant type impractical. Our investigations have unveiled a distinctive ADAM9-KRAS loop that amplifies KRAS activity through a feed-forward mechanism. This unique signaling cascade, which accentuates the effects of KRAS in cancer cells while sparing normal cells, emerges as a viable targetable pathway for therapeutic design. Significantly, our studies demonstrate that ADAM9 suppression augments KRAS degradation across pancreatic cancers harboring both wild-type and mutant KRAS. Notably, the development of ADAM9 inhibitors holds promise as pan-KRAS inhibitors capable of targeting diverse KRAS mutants, presenting a transformative approach to pancreatic cancer treatment (Nature Cancer, 2024). I will expound upon our research discoveries regarding ADAM9 and its profound implications in the realm of cancer therapeutics.

SPEAKERS

Yi-Hung Chen

Professor and Associate Deam
China Medical University

Biography:

Dr. Yi Hung Chen currently holds the positions of Professor and Associate Dean, College of Chinese Medicine, China Medical University in Taichung, Taiwan. He completed his Ph.D. in Pharmacology at the College of Medicine, National Taiwan University. Dr. Chen has also enriched his research experience internationally as a Visiting Scholar in the Department of Pharmacology at Temple University School of Medicine, Philadelphia, USA.

Dr. Chen's research focuses on the intersection of acupuncture and neuroscience, with a particular emphasis on analgesia and neuroprotection. His work explores both basic and clinical aspects, aiming to bridge traditional Chinese medical practices with modern scientific understanding. His notable contributions include elucidating the mechanisms of non-opioid acupuncture analgesia. In 2018, his significant findings on the analgesia pathway via orexin-initiated endocannabinoid disinhibition in the periaqueductal gray, achieved through median nerve stimulation with electroacupuncture, were published in the Proceedings of the National Academy of Sciences of the United States.

Additionally, Dr. Chen has conducted pioneering studies on the neuroprotective effects of electroacupuncture in animal models of Parkinson's disease and dental pulp injury, exploring potential therapeutic pathways involving BDNF, HDAC, and microglial activities. His research excellence has been recognized with several accolades, including the "Outstanding Professor of the China Medical University" award in 2019 and "The Outstanding Research Award of Physician Zhang Butao"in 2021.

Dr. Chen's work continues to contribute to the field of neuroscience, providing valuable insights into the complex mechanisms of acupuncture.

Title: Analgesic and Neuroprotective Effects of Electroacupuncture: Fundamental Insights

Acupuncture, involving the stimulation of specific body points with needles, is used to treat a variety of diseases and has a history of 2500 years. Electroacupuncture (EA), developed in the 1950s for surgical anesthesia, delivers electrical currents through inserted needles, offering therapeutic effects. Recognized by the WHO, acupuncture and EA have demonstrated efficacy in treating various clinical conditions, including pain.

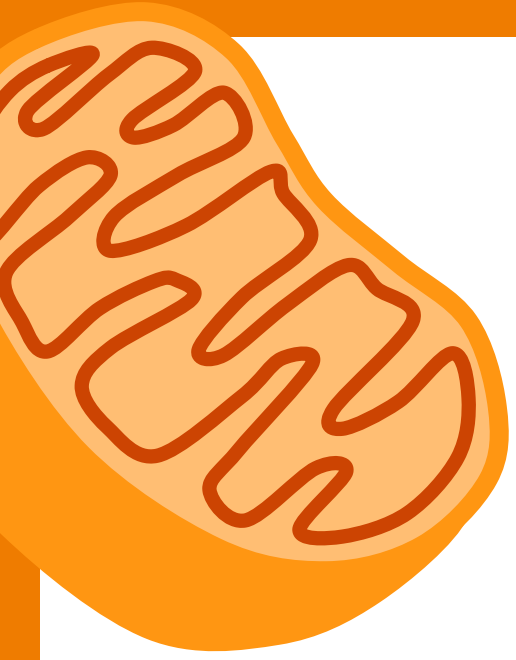
EA is believed to activate peripheral nerves, modulating neurotransmitters in the central nervous system (CNS) to provide pain relief. Early studies linked EA's analgesic effects to endogenous opioids. Recent findings highlight non-opioid mechanisms involving the orexin and endocannabinoid systems, which are independent of endogenous opioids. Glial cells, including microglia and astrocytes, play significant roles in pain and neuroinflammation. EA modulates their activity, reducing the release of pro-inflammatory mediators and thereby alleviating pain. By modulating glial cell activity, EA also offers neuroprotective benefits, particularly in conditions like neuropathic pain and brain injury.

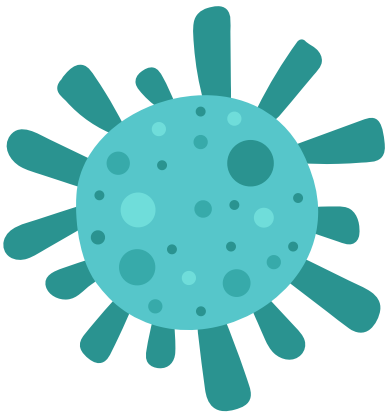
Our recent findings indicate several clinical applications:

- Chronic Pain Management: EA at specific acupoints (e.g., PC6) reduces pain through the orexin-endocannabinoid pathway, beneficial for opioid-tolerant individuals.
- Dental Pain: EA modulates glial cell activity and neuroinflammatory pathways, providing pain relief and attenuating chronic pain development in conditions like irreversible pulpitis.
- Traumatic Brain Injury (TBI): EA treatment demonstrates neuroprotective effects by reducing glial cell activation and neuroinflammation.

In conclusion, electroacupuncture is a promising tool for pain management and neuroprotection.

Its ability to engage both opioid and non-opioid pathways and modulate glial cell activity makes it a valuable pain management strategy.





THANK YOU!

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