Celebrating the 10th Anniversary of the
University of Macau Faculty of Health Sciences
澳門大學健康科學學院十週年院慶

MACAU SYMPOSIUM ON BIOMEDICAL SCIENCES

14 - 17 JUNE 2023

PROGRAMME BOOKLET

UNIVERSIDADE DE MACAU
UNIVERSITY OF MACAU
健康科學學院
Faculdade de Ciências da Saúde
Faculty of Health Sciences

WIFI INFORMATION

SSID:	UM_WLAN_PORTAL	UM_PUBLIC_WIFI
User ID:	msbs2023	N/A
Password:	msbs2023	N/A

Day 1:	**14 June (WED)**	
Venue:	N21 - G013 Lecture Hall	
Session ONE:	澳門大學健康科學學院與浙江大學“一帶一路”國際醫學院醫學交流 Exchange Session on Biomedical Sciences between University of Macau and International School of Medicine, Zhejiang University	
Session Chairs:	Kai MIAO and Aifu LIN	
14:30	Opening Address	**Prof. Chuxia DENG** Dean of the Faculty of Health Sciences of the University of Macau
14:35	Opening Address	**Dr. Wei LI** Deputy Secretary of the Communist Party Committee, The Fourth Affiliated Hospital, Zhejiang University School of Medicine and International School of Medicine, Zhejiang University
From	**Speaker**	**Talk Title**
14:40	**Qiming SUN** Zhejiang University	Cholesterol Metabolism Integrates ER Homeostasis and Innate Immunity
15:00	**Dante NECULAI** Zhejiang University	Excess Plasmalemmal Cholesterol Activates a $G\alpha_q$/$PLC\beta_3$ Relay to Induce the Formation of E-SYT1-dependent ER-PM Contact Sites
15:20	**Xin LI** Zhejiang University	A Conserved Small RNA-based Genome Integrity Protection Mechanism
15:40	**Bingbing WU** Zhejiang University	Endometrial Development and Regeneration
16:00	Coffee Break	
16:30	**Edwin CHEUNG** The University of Macau	Nuclear Receptor Coregulator Function in Nuclear Hormone-Dependent Cancers
16:50	**Gang LI** The University of Macau	Deciphering the Metabolic-epigenetic Crosstalk: AMPK's Impact on TET2 and Transcriptional Regulation of Pax7
17:10	**Fangyuan SHAO** The University of Macau	Reversal of Broad Drug Resistance Through Increasing Mitochondrial OXPHOS to Induce Protein Neosynthesis
17:30	**Guokai CHEN** The University of Macau	Metabolic Regulation on Pluripotency and Cell Fate Determination
18:30	Welcome Reception: Cozinha Pinocchio Taipa	

< End of 14 June >

Day 2:	15 June - AM (THU)	
Venue:	N2 - University Hall	
08:30	Registration Guest Reception	

Opening Ceremony of the 9th Macau Symposium on Biomedical Sciences

09:00	Welcome Remark	**Prof. Yonghua SONG** Rector of the University of Macau
	Address	**Mr. Kun Wai CHEANG** Acting President of the Administrative Committee of the Science and Technology Development Fund
	Programme Introduction	**Prof. Chuxia DENG** Dean of the Faculty of Health Sciences of the University of Macau
	Group Photo	

Plenary Session ONE

Session Chair: Chuxia DENG
Session Co-Chair: Mien-Chie HUNG

From	Speaker	Talk Title
09:30	**Mien-Chie HUNG** China Medical University	Marker-guided Effective Therapy (Mget)
10:10	**Weihong TAN** The Institute of Basic Medicine and Cancer, Chinese Academy of Sciences	Molecular Mapping for Digitizing Single Cell
10:40	**Fan ZHANG** Fudan University	Second Near-Infrared Window Fluorescent Probes for *In Vivo* Multiplexed Bioimaging
11:10	Coffee Break	
11:40	**Liang TONG** Columbia University	Molecular Insights into Human RNA 3'-end Processing and Relevance for Cancer Drug Discovery
12:10	**Yehuda G. ASSARAF** Technion - Israel Institute of Technology	Lysosomal Biogenesis and Exocytosis as A Novel Target to Surmount Cancer Multidrug Resistance
12:40	Luncheon and Poster Session Sponsored by SENG CHUANG YING MEDICAL AND HEALTH EQUIPMENT CO., LTD. Venue: N1 - Multi-function Hall	

Day 2: 15 June - PM (THU)

From: 14:30

Session TWO	**Session THREE**
C. elegans Cell Biology: Membrane, Cytoskeleton and Organelle	Development of Smart Therapeutics and Drug Delivery Systems
Venue: N2 - University Hall	Venue: N1 - Multi-function Hall
Session Chair: Hongjie ZHANG	Session Chairs: Ruibing WANG and Ying ZHENG
Guangshuo OU Tsinghua University Hyperactive Protein Responses and Functional Residuomics of Cilia	**Wei TAO (Online)** Harvard University Nano-/Microscale Materials-enabled Drug Delivery Technologies
Xiaochen WANG Institute of Biophysics, Chinese Academy of Sciences Maintenance of Lysosome Integrity and Function in *C. elegans*	**Jinyao LIU (Online)** Shanghai Jiao Tong University Bacteria-based Therapeutics
Chonglin YANG Yunnan University Understanding Metabolic Damage of Mitochondria	**Zhen GU (Online)** Zhejiang University Bioresponsive Drug Delivery
Anbing SHI Huazhong University of Science and Technology How Cell Stabilizes Endosomal F-actin?	**Feng QIAN** Tsinghua University High Concentration Therapeutic Proteins: From Formulation Optimization To Protein Design
	Changyou ZHAN Fudan University Cutaneous Transport and Toxicity of Liposomal Doxorubixin: The Mechanisms and Clinical Interventions

16:00 Coffee Break and Poster Session

Day 2: **15 June - PM (THU)**

From: 16:30

Session FOUR
Cancer Research and Therapy Development

Venue: N2 - University Hall

Session Chair: Kathy LUO

Hanry YU
National University of Singapore

Contextual AI Approach of Classifying Earlier GI Tract Diseases

Karl TSIM
The Hong Kong University of Science and Technology

Phytochemicals Regulate Angiogenic Functions in Endothelial Cells by Binding to Vascular Endothelial Growth Factor (VEGF): Drug Development Targeting to Cancer Therapy

Peng CHEN
Nanyang Technological University

Imaging Guided Multimodal Cancer Therapy Based on Nano-Multizymes

G. J. (FRITS) PETERS
Amsterdam University Medical Centers

Co-cultured Spheroids as Model Systems for Tumour Micro-environment and Drug Testing

Kathy LUO
The University of Macau

Elucidating How Circulating Tumor Cells Resist Fluidic Shear Stress in Circulation and Acquire Stronger Metastatic Capacities

Session FIVE
Biology of Aging

Venue: N1 - Multi-function Hall

Session Chair: Wakam CHANG

Co-Chair: Garry WONG

Zhongjun ZHOU
The University of Hong Kong

Disorganized Chromatin Hierarchy Drives Stem Cells Aging in Atypical Laminopathy-based Progeria Mandibuloacral Dysplasia Type A

Yidong SHEN
Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences

The Trigger of the Germline Longevity

Haiying LIU
Sun Yat-Sen University

Telomere Stability Regulation and Cellular Senescence

18:30 Gala Dinner: Tack Hsin Restaurante

< End of 15 June >

Day 3: 16 June - AM (FRI)

From: 09:00

Session SIX
Drug Discovery and Biomaterials for Immune Regulation

Venue: N2 - University Hall
Session Chairs: Yunlu DAI, Joong Sup SHIM

Yongjun DANG
Chongqing Medical University
Discovery of Small Molecules for Tumour Immuno-Regulation

Liang CHEN
Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences
Proteostasis and Antitumour Immunity

Daishun LING
Shanghai Jiao Tong University
Dynamic Nano-Assemblies-based Biomaterials and Drug Delivery Systems

Haijun YU
Shanghai Institute of Materia Medica, Chinese Academy of Sciences
Smart Nanomedicine for Cancer Immunotherapy

Chengtie WU (Online)
Shanghai Institute of Ceramics, Chinese Academy of Sciences
3D Printing of Biomimetic Biomaterials and Cells

Session SEVEN
Stem Cell, Gene and Cell Therapy

Venue: N1 - Multi-function Hall
Session Chair: Guokai CHEN
Co-Chair: Ren-He XU

Ji DONG
Bioland Laboratory, Guangzhou
A Single-nucleus Survey of Mammalian Hibernation for Liver Protection

Junjiu HUANG
Sun Yat-Sen University
Gene Editing Therapy of β-Thalassemia

Wanze CHEN
Shenzhen Institute of Synthetic Biology and Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences
Live-seq Enables Temporal Transcriptomic Recording of Single Cells

Xiao Yang ZHAO
Southern Medical University
Understanding and Managing of Male Infertility Based on Mechanism Study

10:30 Coffee Break and Poster Session

From: 11:00

Session EIGHT
Cell Death

Venue: N2 - University Hall
Session Chair: Hanming SHEN

Liming SUN
Institute of Biochemistry and Cell Biology and Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences
Necroptosis on the Brake

Sudan HE
Suzhou Institute of Systems Medicine
Cell Death-Dependent and -Independent Functions of RIPK1/RIPK3 in Inflammatory Diseases

Session NINE
G Protein-coupled Receptor: Structure, Signaling and Diseases

Venue: N1 - Multi-function Hall
Session Chair: Leo LEE
Co-Chair: Yang DU

Yang DU
The Chinese University of Hong Kong, Shenzhen
Structure, Function and Drug Discovery of G Protein-coupled Receptor in Nervous System

Sookja Kim CHUNG
Macau University of Science and Technology
Exchange Proteins Activated by Cyclic AMP and Their Role in Diverse Function and Diseases

You-Sun KIM
Ajou University
Necroptosis: Molecular Mechanisms and Disease Implications

Hsien-Da HUANG
The Chinese University of Hong Kong, Shenzhen
Multi-omics in MicroRNA-related Biomarker and Drug Target Discovery

Francis Kaming CHAN
Zhejiang University
Immunogenic Cell Death: The Good, the Bad and the Ugly

Pei-Gen REN
Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences
Development of Oral Polypeptide Drug Targeting GPRC6A for Nonalcoholic Steatohepatitis

Yung Hou WONG
The Hong Kong University of Science and Technology
Preferential Binding of G Protein to the MT1 Protomer of the MT1/MT2 Heterodimeric Melatonin Receptor Complex

12:30 Luncheon and Poster Session
Sponsored by Thermo Fisher Scientific (Hong Kong) Limited
Venue: N1 - Multi-function Hall

14:30 Coffee Break and Poster Session
Venue: N1 – Multi-function Hall

From: 16:30

Session TEN
Molecular Mechanism and Precise Diagnosis and Treatment of Cancer

Venue: N2 - University Hall
Session Chair: Kai MIAO

Yuan LIU
Institute of Basic Medicine and Cancer, Chinese Academy of Sciences
Nanoproteomics-based Biomarker Discovery and Cancer Diagnostics

Jiangjiang QIN
Institute of Basic Medicine and Cancer, Chinese Academy of Sciences
Targeting UPS for Cancer Therapy: New Mechanisms and New Strategies

Xiangsheng LIU
Institute of Basic Medicine and Cancer, Chinese Academy of Sciences
Tumour Targeting Aptamer Drug Conjugate and Nano Drug Delivery System

Ji JING
Institute of Basic Medicine and Cancer, Chinese Academy of Sciences
Design Optogenetic Toolbox for Deep Understanding Intracellular Organelles Communications and Remote Control of Programmed Cell Death

Session ELEVEN
Spatial Omics Biology

Venue: N1 - Multi-function Hall
Session Chairs: Edwin CHEUNG and Peng WANG

Longqi LIU
BGI Genomics
Large-field of View, High-Resolution Spatially Resolved Transcriptomics Using DNA Nanoball Patterned Array

Xianting DING
Shanghai Jiao Tong University
Single Cell Proteomic Analysis Techniques and Clinical Applications

Xiang ZHOU
University of Michigan
Statistical Methods for Spatial Transcriptomics

< End of 16 June >

Day 4: **17 June - AM (SAT)**

From: 09:00

Session TWELVE
Natural Product-based Drug Discovery

Venue: N2 - University Hall

Session Chairs: Xiuping CHEN and Ying WANG

Hong PENG (Online)
Yale University

Roles of University Technology Transfer in Biomedical Business

Jinhua WANG (Online)
Peking Union Medical College

The Study on Anti-Glioblastoma Effect and Its Mechanism of Sinomenine Ester Derivative

Hubing SHI
Sichuan University

Immune Checkpoint HLA-E:CD94-NKG2A Mediates Evasion of Circulating Tumour Cells from NK Cell Surveillance

Liwu FU
Sun Yat-Sen University

Progress in the Personalization of Tumour Chemotherapeutic Drug

Hoi Leong Xavier WONG
Hong Kong Baptist University

Therapeutic Targets of Metabolic Disorders - What's New?

Session THIRTEEN
Targeting Gut Microbiota and Metabolism for Cancer Immunomodulation

Venue: N1 - Multi-function Hall

Session Chair: Elaine LEUNG

Xiang ZHANG
The Chinese University of Hong Kong

Gut Microbiota, Metabolites and Fatty Liver Diseases

Yuting YANG on behalf of Hong WEI
Sun Yat-Sen University

Humanized Germ-free Animal Models and Their Roles in the Study of Microbiome Related Tumour Genesis and Development and Immunotherapy

Di LIU
Wuhan Institute of Virology, Chinese Academy of Sciences

Intestinal Microbiome and Disease Health

Carmen Chak-Lui WONG
The University of Hong Kong

Precision Medicine and the Mechanistic Basis of Combination Treatments for Liver Cancer

10:30 Coffee Break and Poster Session

Day 4: 17 June - AM (SAT)

From: 11:00

Session FOURTEEN
Molecular Probes and Biosensors

Venue: N2 - University Hall

Session Chairs: Xuanjun ZHANG and Xiaoqiang CHEN

Zhizeng GAO
Sun Yat-Sen University
Development of Fluorescent Polarization-based High Throughput Screening Assays

Zonghai SHENG
Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences
Recent Advances in ICG Near-Infrared Fluorescence Molecular Imaging in the Second Biowindow

Xiaoqiang CHEN
Nanjing Tech University
Functional Dyes for Imaging and Detection Applications

Peng GUO
Institute of Basic Medicine and Cancer, Chinese Academy of Sciences
Spatiotemporal Visualization of Bystander Activity of Antibody Drug Conjugates for Enhancing Solid Tumour Penetration

Session FIFTEEN
Neuroscience, Aging and Degenerative Diseases

Venue: N1 - Multi-function Hall

Session Chair: Wenhua ZHENG
Co-Chair: Jiangang SHEN

Qing WANG
Southern Medical University
Neurovascular Unit Roles in Neurodegeneration

Xintong LIU
Guangdong No. 2 General Hospital
Research Progress in Prehospital Neuroprotection of Acute Stroke

Xifei YANG
Shenzhen Center for Disease Control and Prevention
Adiponectin Deficiency Accelerates Brain Aging via Mitochondria-associated Neuroinflammation

Haiwei HUANG
Sun Yat-Sen University
Effect of Vestibular Dysfunction on Cognition

Jiangang SHEN
The University of Hong Kong
Hypochlorous Acid Derived from Microglial Myeloperoxidase Mediates High-mobility Group Box 1 Release from Neurons to Amplify Brain Damage in Cerebral Ischemia-reperfusion Injury

12:30 Luncheon and Poster Session
Sponsored by LingBio Biotechnology Macau Company Ltd
Venue: N1 - Multi-function Hall

Day 4: 17 June - AM (SAT)

Venue: N2 - University Hall

Plenary Session TWO

Session Chair: Chuxia DENG

Session Co-Chair: Han Ming SHEN

From	Speaker	Talk Title
14:30	**Dennis LO** The Chinese University of Hong Kong	Creating Paradigms Shift in Molecular Diagnostics
15:10	**Alexander HOFFMANN** University of California, Los Angeles	A Temporal Signaling Code to Specify Immune Responses
15:40	**Gourisankar GHOSH** University of California San Diego	Diverse Nuclear Factors are Enablers of NF-κB's Transcriptional Activity
16:10	Coffee Break	
16:40	**Hong ZHANG** Institute of Biophysics, Chinese Academy of Sciences	Liquid–liquid Phase Separation in Autophagy
17:10	**Richard J. YOULE** National Institute of Neurological Disorders and Stroke, National Institutes of Health	Mitochondria Quality Control and Parkinson's Disease
17:40	Short Talks for Best Poster Awards	
18:10	Poster Award Ceremony	

Closing Ceremony of the 9th Macau Symposium on Biomedical Sciences

18:20	Closing Speech	**Prof. Ren-He XU** Associate Dean (Research) of the Faculty of Health Sciences of the University of Macau

< End of 17 June >

Exchange Session on Biomedical Sciences between University of Macau and International School of Medicine, Zhejiang University

Session Chairs: Kai MIAO and Aifu LIN

Cholesterol Metabolism Integrates ER Homeostasis and Innate Immunity

Qiming SUN

Zhejiang University

Biography:

Qiming obtained his PhD degree in Biochemistry from Nanjing University in 2006. He received postdoc training at University of California at Berkeley and Harvard Medical School in the US. Then he Joined Zhejiang University in 2014. His lab studies the basic biology of organelle hemostasis regulated by canonical and non-canonical autophagy, as well as how the dysfunction of these pathways is connected to tumourigenesis, metabolic syndromes, infectious disease, and neurodegeneration. His research has made many contributions to autophagy and related field, which led to more than 30 scientific publications.

Abstract:

The endoplasmic reticulum (ER) plays a pivotal role in regulating cholesterol metabolism and controlling the STING-mediated innate immune response. However, it remains unclear how the STING signaling pathway is spontaneously or excessively activated in situations where cholesterol is depleted or at low levels. We found that cholesterol directly binds to the cholesterol sensor SCAP and an ER-phagy receptor. This binding regulates their interaction with STING. Cholesterol overload counteracts the activating effect on STING. *In vivo* assays further demonstrate that this signaling axis integrates cholesterol metabolism and innate immunity.

Excess Plasmalemmal Cholesterol Activates a Gαq/PLCβ3 Relay to Induce the Formation of E-SYT1-dependent ER-PM Contact Sites

Dante NECULAI

Zhejiang University

Biography:

Dante Neculai is a professor of Cell Biology at Zhejiang University in China. He received his BSc and MSc in Chemistry from the University of Bucharest, Romania, and his PhD in Chemistry from the University of Göttingen, Germany. Prof. Neculai's research focuses on innate immunity, immunometabolism, and host-pathogen interactions, with an emphasis on pattern recognition receptors and lipid metabolism regulation. He has published over 33 articles in respected journals and has been recognized with multiple awards and research grants. Prof. Neculai's interdisciplinary background spans organic synthesis, structural biology, and molecular cell biology, which has allowed him to make significant contributions to understanding lipid metabolism and its role in innate immunity.

Abstract:

Lipid droplets (LDs) are evolutionarily conserved organelles specialized in the storage of neutral lipids, cholesterol esters and triglycerides, thereby protecting protect cells from the toxicity of excess cholesterol and fatty acids while allowing for mobilization of these stores in times of nutrient deprivation. Defects in LD function are associated with obesity and many human diseases, including nonalcoholic fatty liver, lipodystrophy and neutral lipid storage disorders. Cysteine palmitoylation (S-palmitoylation) is a reversible post-translational modification that occurs on thousands of mammalian proteins yet how this modification influences physiology remains poorly understood. Here we find that the palmitoyltransferase zDHHC11 modulates LD homeostasis and that disruption of zDHHC11 function phenocopies the loss of LD-associated triglyceride lipase ATGL. We further demonstrate that S-palmitoylation of ATGL on Cys15 is mediated by zDHHC11 and that zDHHC11 is required for ATGL function under basal and starvation conditions in human cells and murine liver. Our study identifies a critical zDHHC11-ATGL axis in regulating mammalian lipid metabolism.

A Conserved Small RNA-based Genome Integrity Protection Mechanism

Xin LI

Zhejiang University

Biography:

Prof. Li received his undergraduate degree from the Department of Biological Sciences and Technology, Tsinghua University, and his PhD degree from Cornell University, USA. He has led three National Institutes of Health (NIH) and one U.S. Department of Agriculture research projects with a total of $3.3 million in funding, and has participated in many major project reviews in the U.S. and Europe. His research has been published in more than 20 top journals including *Nature Cell Biology*, *Nature Communications*, *Poultry Science*, and *Biology of Reproduction*. He has published in more than 20 top professional journals with average impact factor IF>10 and one patent application with Melissa Moore. He has been invited to give nearly 60 presentations at international conferences and prestigious universities. His laboratory has completed the training of more than 40 postdoctoral, doctoral and master's degree holders, medical doctors and undergraduates.

Abstract:

Unlike PIWI-interacting RNA (piRNA) in other species that mostly target transposable elements (TEs), >80% of piRNAs in adult mammalian testes lack obvious targets. However, mammalian piRNA sequences and piRNA-producing loci evolve more rapidly than the rest of the genome for unknown reasons. Here, through comparative studies of chickens, ducks, mice, and humans, as well as long-read nanopore sequencing on diverse chicken breeds, we find that piRNA loci across amniotes experience: (1) a high local mutation rate of structural variations (SVs, mutations ≥50bp in size); (2) positive selection to suppress young and actively mobilizing TEs commencing at the pachytene stage of meiosis during germ cell development; and (3) negative selection to purge deleterious SV hotspots. Our results indicate that genetic instability at pachytene piRNA loci, while producing certain pathogenic SVs, also protects genome integrity against TE mobilization by driving the formation of rapid-evolving piRNA sequences.

Endometrial Development and Regeneration

Bingbing WU

Zhejiang University

Biography:

Bingbing Wu, PhD Junior PI at the Fourth Affiliated Hospital of Zhejiang University School of Medicine, Zhejiang University,graduate student tutor of obstetrics and gynecology, Research interests: Stem progenitor cells for endometrial development and regeneration and the differentiation regulatory mechanisms, presided National Natural Science Foundation projects, published papers in Cell Discovery, Biomaterials, Stem Cell Reports and other mainstream regenerative medicine journals as the first author, co-first and corresponding author.

Abstract:

Large scale damage to the basal layer of the endometrium will lead to intrauterine adhesions, which is a great challenge in clinic. Tissue engineering technology is expected to achieve endometrial regeneration, but the acquisition of pro-regenerative cell and *in vitro* large-scale expansion of endometrial lineage face challenges, and the deep-seated reason is that the key scientific issues of "cell source and differentiation regulation of endometrial development and regeneration" are not fully studied, and there is a lack of enough knowledge of endometrial lineage-promoting cell markers and differentiation regulation. The speaker focuses on endometrial regeneration and repair research. Main findings: 1. Discovery of new pro-regenerative cell subpopulations in the process of endometrial development and regeneration; 2. Analysis the differentiation, regulation and regeneration mechanism of the newly discovered pro-regenerative cells; 3. Establishment of new technologies for tissue engineering to promote endometrial regeneration based on developmental and regenerative factors.

Nuclear Receptor Coregulator Function in Nuclear Hormone-Dependent Cancers

Edwin CHEUNG

The University of Macau

Biography:

Prof. Edwin Cheung received his bachelor's degree in molecular biology from UC Berkeley in 1998 and his PhD degree from University of Manchester in 2004. He received a Susan G. Komen Breast Cancer Foundation postdoctoral fellowship while working at Cornell University. He spent 9 years as a Senior Investigator at the Genome Institute of Singapore. During this time, he also held adjunct positions at the National University of Singapore and Nanyang Technological University. In 2013, he joined the University of Macau as a Professor in the Faculty of Health Sciences. Prof. Cheung is currently on the editorial board of Molecular Cancer Research. Prof. Cheung is an international leader in the field of nuclear hormone signaling and has published over 50 papers in top journals such as *Nature*, *Nature Genetics*, *Cell*, *Genome Research*, and *EMBOJ*.

Abstract:

We are interested in understanding the molecular details of nuclear hormone signaling and how these pathways relate to disease conditions, including cancers. Specifically, we are investigating how lipophilic hormones such as estrogens and androgens regulate the transcriptional activities of nuclear hormone receptors in a chromatin environment. We use multi-omics approaches, including proteomics and next-generation sequencing, to define the molecular mechanisms of transcriptional regulation by estrogen and androgen receptors. In this presentation, I will highlight some of our recent coregulator findings on nuclear receptor transcriptional activity and hormone-dependent cancer biology. Together, the results from our work have direct implications for the development of therapeutic targets for the wide range of diseases and disorders in which these and other nuclear receptors play a role.

Deciphering the Metabolic-epigenetic Crosstalk: AMPK’s Impact on TET2 and Transcriptional Regulation of Pax7

Gang LI

The University of Macau

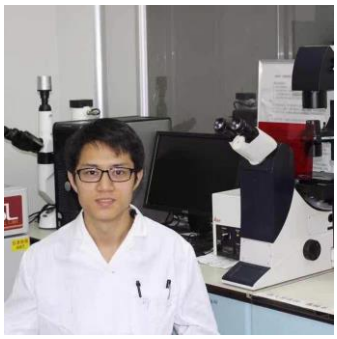
Biography:

Prof. Gang Li serves as an Associate Professor at the University of Macau's Faculty of Health Sciences (FHS) and holds positions on the Chinese Preventive Medicine Association's bioinformatics committee and Scientific Reports' editorial board. Prof. Li's lab focuses on epigenetic regulators' posttranslational modifications and cancer epigenetics, employing an interdisciplinary approach that includes biochemistry, mouse genetics, next-generation sequencing, and bioinformatics. A notable discovery by his team involved a Histone H3 mutation that activated Cancer/Testis antigens in childhood brain tumours, presenting potential immunotherapeutic targets. Prof. Li's research also revealed AMPK's role as a cell's central energy sensor, modifying the epigenome by phosphorylating epigenetic regulators like TET2. Furthermore, his lab is investigating cancer therapies by targeting AMPK and developing bioinformatic tools, such as TFmapper and GenekitR, for mining gene expression omnibus datasets. Prof. Li has authored around 90 papers in scientific journals, garnering over 3,300 citations.

Abstract:

Our work reveals a signaling link between metabolism and the epigenome, where metabolic regulator AMPK phosphorylates and stabilizes epigenetic modifier TET2. We also demonstrate the AMPK-TET2 axis's role in regulating Pax7 transcription, a key gene in muscle cell development and differentiation. Loss of AMPK activity led to decreased global 5hmC levels, differentiation defects in C2C12 cells, and a significant reduction in Pax7 expression. This correlated with increased DNA methylation at genic and enhancer regions in AMPK-null myoblasts and myotubes. We identified a novel enhancer, hypermethylated in AMPK-null cells, that regulates Pax7 expression in both cell and mouse models. The findings emphasize the complex interplay between the AMPK regulatory network and the epigenome, underscoring the need for further research to explore metabolic regulators' impact on the epigenome for improved disease prevention and treatment.

Reversal of Broad Drug Resistance Through Increasing Mitochondrial OXPHOS to Induce Protein Neosynthesis



Fangyuan SHAO

The University of Macau

Biography:

Prof. Fangyuan SHAO received his PhD in University of Macau. After being adopt by the UM Macao Talent Program as Post-doctoral Fellowship. He is now the Research Assistant Professor in Faculty of Health Sciences, University of Macau. His research mainly focuses on the mechanism study of anticancer drug induced protein damage and develop treatment strategy for overcoming multidrug resistant. Through proteasome detection kit and drug combination strategy, he devotes to develop safer and more efficient theranostic system for the breast and colorectal cancer.

Abstract:

Treatment with one type of drug frequently resulted in broad drug resistance. Our previous study demonstrated that damaged protein clearance serves as a novel mechanism of broad drug resistance. In this study, we further demonstrate that anticancer drug treatment widely induces protein damage, which is much more prevalent than DNA damage. Further mechanism study indicate that ribosome mediated protein synthesis is the major source of drug induced protein damage. We also find that drug induced protein damage has close relationship with cell cycle distribution, and drug resistant cancer cells are characterized as slow cycling and largely quit the cell dividing phases. Further study indicate that mitochondrial activity played a major role in drug induced protein damage between different cell cycle, which is mediated by the regulation of the proteasome activity and protein synthesis rate. Enhanced mitochondrial respiration through inhibition of pyruvate dehydrogenase kinase 1 (PDK1) disrupted the slow cycling state and increased protein damage. Further combination with proteasome inhibitor completely block protein damage clearance in the cancer resistant cells and overcome broad drug resistance through induction of protein damage.

Metabolic Regulation on Pluripotency and Cell Fate Determination

Guokai CHEN

The University of Macau

Biography:

Dr. Guokai Chen is a Professor in the Faculty of Health Sciences at University of Macau. Dr. Chen's group focus on technology development for human pluripotent stem cells (hPSC) and their clinical applications. He has developed the next generation of hPSC culture condition and differentiation methods to produce functional cells for potential cell therapy. Dr. Chen's inventions have been widely used in stem cell field, including E8 cell culture system.

Abstract:

Human pluripotent stem cells (hPSCs) can differentiate to all cell types in the body, and they have great potential in regenerative medicine. It is hotly discussed topic in stem cell field how metabolism regulates cell fate determination. It is commonly believed that metabolism acts through epigenetic pathway. Our studies show that signaling pathways are important downstream effector of metabolism. We demonstrate that pluripotency state is not affected by the level of de novo lipogenesis. Signaling molecule lysophosphatidic acid (LPA) shifts metabolic and transcriptome landscapes, leading to novel stem cell state. Meanwhile, we find that stem cells modify their own microenvironment with autocrine lactic acid from glycolysis, which profoundly influences cell survival and cell fate determination. These studies reveal novel aspects of molecular regulation and provide new solutions for stem cell application.

Plenary Session ONE

Session Chair: Chuxia DENG
Session Co-Chair: Mien-Chie HUNG

Marker-guided Effective Therapy (Mget)

Mien-Chie HUNG

China Medical University

Biography:

Mien-Chie Hung, PhD is the President for China Medical University and the Chancellor for China Medical University - Asia University System in Taichung, Taiwan. He was vice president for basic research and professor and chair of the Department of Molecular and Cellular Oncology at The University of Texas MD Anderson Cancer Center. Dr. Hung 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. Up to date, Dr. Hung has published more than 600 peer-reviewed articles. His lifetime h-index reaches to 163 (Google Scholar). Dr. Hung was inducted as an Academician of the Academia Sinica in Taiwan in 2002 and as a Fellow in Biological Sciences section, American Association for the Advancement of Science in 2010. He serves in numerous prestigious award committees including Selection Committee for Tang Prize in Biopharmaceutical Science.

Abstract:

Anti-PD-1/PD-L1 therapy is a promising approach in cancer therapy, we showed that glycosylation of PD-L1 is required for its protein stability and interaction with PD-1 (*Nature Comm* 2016). Currently, we have developed monoclonal antibodies against glycosylation-specific PD-L1/PD-1, and an impressive therapeutic effect was observed through antibody-drug-conjugate approach (*Cancer Cell* 2018a & *Cancer Res* 2020) as well as CAR-T. 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) and Tyro 3 (J *Clin Invest* 2021). In addition, PARP inhibitors resistant mechanism was identified and effective combination therapy was developed by targeting ALK/CDK9-Y19 pathway (*Nature Cancer* 2022). This talk will include our discoveries on developing therapies for lung, pancreatic cancers, and HCC (*Cancer Cell* 2018b, *Cancer Cell* 2018c *Nature* 580:530, 2020) as well as a new methodology to retrieve antigen by protein deglycosylaton to measure accurately the PD-L1 level in the surface of tumours then using it as a biomarker for immunotherapy (*Cancer Cell* 2019, *AJCR* 2022). Multiple new advances of anti-PD-L1/ PD-1 that have recently been developed were summarized in the literature (*Nat. Rev. Clin. Oncol* 2022). A novel PD-L1 function that is independent of its role in immune checkpoint, namely PD-L1 in the nucleus harbors a nuclear transcriptional activity and promotes tumour pyroptosis downstream of TNFα (*Nat. Cell Biol* 2020; *Mol Cell* 2021). During the pandemic, the research team at China Medical University in Taichung has successfully used our experience and expertise in cancer-targeted therapy to target SARS-CoV-2. We will share our progress on development of inhibitors on the SARS-CoV-2, including natural products: tannic acid (*AJCR* 2020a) and Peimine (*J. Food Biochem* 2022); FDA-approved drugs: Flupirtine (*AJCR* 2021), Disulfiram (*AJCR* 2022), Imatinib (*Int J Mol Sci.* 2021), Tafenoquine (*JBC* 2022). A set of traditional herbal medicine and coffee leaf extract was shown to inhibit different strains of SARS-CoV-2 infectivity (*AJCR* 2020c and *IJBS* 2022). Some of these compounds are currently being tested in the clinical trials.

Molecular Mapping for Digitizing Single Cell

Weihong TAN

The Institute of Basic Medicine and Cancer, Chinese Academy of Sciences

Biography:

Professor Weihong Tan earned his PhD in physical chemistry at the University of Michigan in 1993. Currently, he is the director of Hangzhou Institute of Medicine, Chinese Academy of Sciences, the dean of the Cancer Hospital of the University of Chinese Academy of Sciences. He is also the director of the State Key Laboratory of Chemo/Biosensing and Chemometrics, and distinguished professor of chemistry and biology at Hunan University, and the director of the Institute of Molecular Medicine at Renji Hospital and Shanghai Jiao Tong University. He served as a University Distinguished Professor and a V.T. and Louis Jackson Professor at the University of Florida for more than 20 years. Professor Tan's research is in the general area of bioanalytical chemistry, molecular medicine and chemical biology. He specializes in aptamer research, DNA nanotechnology, and cancer theranostics.

Abstract:

The development of science and technology has enabled human understanding of oneself to enter the molecular level.Mapping every molecule of the cell will transform our understanding of biology and disease and could lead to major advances in disease diagnosis, treatment, and prevention. As an important component of cells, the cell membrane contains a rich array of disease biomarkers and drug targets that play an extremely important and unique role in the precision medicine. Therefore, a comprehensive molecular analysis of the cell membrane surface is the foundation for achieving disease molecular typing and "facial recognition-style" multi-parameter precision diagnosis and treatment. Our team has pioneered a new method for screening nucleic acid aptamers using intact cells as screening targets, called Cell-SELEX, to address the bottleneck of a lack of effective molecular recognition tools for the cell membrane surface. This method allows for the in situ screening of multiple target molecules on living cells under unknown conditions, and has identified multiple membrane protein markers, providing targets for precision diagnosis and treatment. These aptamers have been widely applied in biomedical research, including ultra-sensitive detection of tumours, molecular imaging, and targeted drug delivery. Recently, our group has developed a new technology of translating the great power of high-throughput gene sequencing into the ability of molecular profiling of cell membrane proteins using cell-binding aptamers to map the cell membrane protein at single cell resolution. This report will introduce our important progress in using aptamers to map the molecular landscape of cell surfaceome, and explore their value in cancer molecular subtyping and precision medicine.

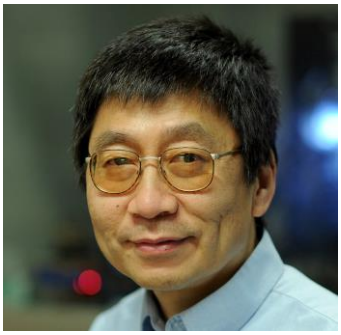
Second Near-Infrared Window Fluorescent Probes for *In vivo* Multiplexed Bioimaging

Fan ZHANG
Fudan University

Biography:
Fan Zhang received his PhD degree in 2008 in Department of Chemistry, Fudan University. After a postdoctoral fellowship in the University of California, Santa Barbara, he was promoted as Associate Professor in Fudan University in 2010 and then Professor in 2013. His researches are funded by NSFC and Shanghai Government, etc. Till now, he has published more than 100 papers as corresponding/first author, including Nat. Mater., Nat. Nanotechnol., Nat. Commun., J. Am. Chem.Soc., Angew. Chem. Int. Ed., with over 30,000 citations, H Index 92. Over 30 papers were selected in ESI "Highly Cited Papaers". From 2018-2021, he was selected as the High Cited Researchers of Clarivate Analytics.

Abstract:
Deep tissue imaging in the second near-infrared (NIR-II) window holds great promise for physiological studies and biomedical applications. However, inhomogeneous signal attenuation due to biological matter hampers the application of multiple-wavelengths NIR-II probes to multiplexed imaging. Here we present lanthanide-doped NIR-II nanoparticles with engineered luminescence lifetimes for *in vivo* quantitative imaging using time-domain multiplexing. To achieve this, we devise a systematic approach based on controlled energy relay that creates a tunable lifetime range spanning 3 orders-of-magnitude upon a single emission band. We consistently resolve selected lifetimes from the NIR-II nanoparticle probes at depths up to 8 mm in biological tissues, where signal-to-noise ratio derived from intensity measurements drops below 1.5. We demonstrate that robust lifetime coding is independent of tissue penetration depth, and we apply *in vivo* multiplexing to identify tumour subtypes in living mice. Our results correlate well with standard ex vivo immunohistochemistry assays, suggesting that luminescence lifetime imaging could be used as a minimally invasive approach for disease diagnosis.

Molecular Insights into Human RNA 3’-end Processing and Relevance for Cancer Drug Discovery



Liang TONG

Columbia University

Biography:

Liang Tong is currently the William R. Kenan, Jr. Professor in the Department of Biological Sciences, Columbia University, New York. He received his BSc from Peking University, PhD from University of California, Berkeley, and post-doctoral training at Purdue University, Indiana. He joined Boehringer Ingelheim Pharmaceuticals, Connecticut, in 1992, where he established the first structure-based drug design laboratory in the company. He moved to Columbia in 1997, served as Department Chair from 2013 to 2019, and established a vigorous research program in structural biology. He has made fundamental contributions to understanding the molecular mechanisms of many biological systems, especially metabolic enzymes and proteins involved in RNA processing. He has many papers in journals of the highest impact (*Nature, Science* and *Cell*), out of more than 310 publications (h-index 90). He was elected a Fellow of the American Association for the Advancement of Science in 2009, and a Fellow of the American Crystallographic Association in 2021.

Abstract:

Two different machineries are involved in the 3’-end processing of mRNA precursors (pre-mRNAs). Most eukaryotic pre-mRNAs are cleaved and then polyadenylated at the 3’-end, and their processing machinery (the canonical machinery) is composed of CPSF (cleavage and polyadenylation specificity factor), CstF (cleavage stimulation factor), poly(A) polymerase (PAP), CF I (cleavage factor I), CF II, RBBP6, and other protein factors, with a total molecular weight of about 1.8 MDa. In comparison, metazoan replication-dependent histone pre-mRNAs are cleaved at the 3’-end but are not polyadenylated, and their processing machinery is the U7 snRNP, with a total molecular weight of about 1 MDa. CPSF73 is the endoribonuclease for the cleavage reaction in both machineries, and recent studies suggest CPSF73 is also a potential target for novel anti-cancer drugs. We have been studying the molecular basis for the functions of these machineries, and have determined the structures of their protein factors and sub-complexes over the years, including the recent structure of a reconstituted, active U7 snRNP in complex with a model histone pre-mRNA substrate, with the machinery poised for the cleavage reaction. This structure has provided unprecedented molecular insights into pre-mRNA 3’-end processing.

Supported by a grant from the NIH (R35GM118093).

Lysosomal Biogenesis and Exocytosis as A Novel Target to Surmount Cancer Multidrug Resistance

Yehuda G. ASSARAF

Technion - Israel Institute of Technology

Biography:

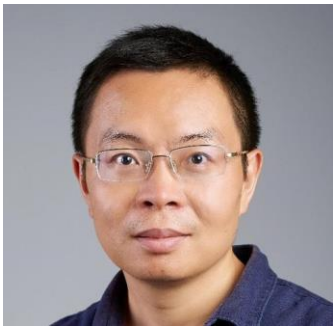
As described below in the section “Contributions to Science” we have been conducting cancer research since 1986 and have made important contributions in the field of molecular basis of drug resistance to cancer therapeutics as well as development of novel treatment modalities to overcome cancer chemoresistance. These include the functional reconstitution of the multidrug resistance efflux transporter P-glycoprotein in proteoliposomes and unravelling its multidrug extrusion capacity from within the lipid bilayer. Furthermore, we have made key contributions to the deciphering of antifolate resistance in leukemia and solid tumours by uncovering loss of function mutations in the reduced folate carrier (RFC), the key influx transporter of antifolate anticancer drugs. Furthermore, we identified a novel modality of chemoresistance to hydrophobic weak base chemotherapeutics, based on their sequestration in lysosomes, hence provoking lysosomal biogenesis and drug extrusion via lysosomal exocytosis of their drug cargo. In the past decade in collaboration with Prof. Livney’s lab, we have also been developing novel targeted nanoparticles that specifically target well-defined cancers, thereby surmounting cancer multidrug resistance.

Abstract:

Anticancer drug resistance constitutes the primary impediment towards curative cancer therapy. Whilst some mechanisms of chemoresistance have been well characterized, multiple molecular mechanisms of drug resistance remain elusive. In this respect, passive ion trapping-based lysosomal sequestration of multiple hydrophobic weak-base chemotherapeutics termed lysosomotropic agents was found to hinder the accessibility of these cytotoxic agents to their cellular target sites, resulting in a markedly reduced cytotoxic activity and drug resistance. We have previously demonstrated that lysosomal sequestration of hydrophobic weak base drugs which relies on the acidic pH of lysosomes, triggers TFEB-mediated lysosomal biogenesis, resulting in an enlarged lysosomal compartment, capable of further enhancing drug sequestration. This lysosomal drug sequestration was followed by lysosomal exocytosis, hence extruding the entrapped drug cargo out of cancer cells. We further showed that cancer cells with an increased number of drug-accumulating lysosomes are more resistant to lysosome-sequestered cytotoxic drugs, resulting in drug-induced lysosome-mediated chemoresistance. Apart from this passive intralysosomal drug sequestration of hydrophobic weak base chemotherapeutics, other mechanisms of lysosome-mediated drug resistance have also been reported; these include active lysosomal drug sequestration mediated by ATP-driven transporters from the ABC superfamily, and a role for lysosomal copper transporters in cancer resistance to platinum-based chemotherapeutics. As abovementioned, we have shown that lysosomal exocytosis is a mechanism facilitating the clearance of chemotherapeutics which highly accumulated in lysosomes, thus providing an additional line of drug resistance, supplementing the organelle entrapment of chemotherapeutics away from their cellular target sites. Along with these mechanisms of lysosome-mediated drug resistance, several modalities were developed for the overcoming of multidrug resistance or exploiting lysosomal drug sequestration, including lysosomal photodestruction and drug-induced lysosomal membrane permeabilization. In the current lecture, I will address the role of acidic lysosomes in mediating cancer multidrug resistance as well as novel modalities to overcome this unique mechanism of chemoresistance.

Session TWO
C. elegans Cell Biology: Membrane, Cytoskeleton and Organelle

Session Chair: Hongjie ZHANG



Hyperactive Protein Responses and Functional Residuomics of Cilia

Guangshuo OU

Tsinghua University

Biography:

Dr. Guangshuo Ou is a Professor and the Associate Dean at the School of Life Sciences, Tsinghua University, Beijing, China. The Ou lab studies the molecular and cellular regulations of cilium formation and ciliopathies. Dr. Ou received his PhD in Cell and Developmental Biology under the guidance of Dr. Jon Scholey at the University of California, Davis (2006). Dr. Ou was a Damon Runyon Postdoctoral Fellow with Dr. Ron Vale at the University of California, San Francisco (UCSF, 2007~2011). Dr. Ou started his independent position as an awardee of the Junior One Thousand Talents Program at the Institute of Biophysics, Chinese Academy of Science, in February 2011. The Ou lab was relocated to Tsinghua University in August 2013. The research findings from the Ou lab have been published in *Science*, *Nature Biotechnology*, *EMBO* Journal, *Developmental Cell*, *Journal of Cell Biology*, *Current Biology*, *PNAS*, and other journals. The Chinese National Science Foundation awarded Dr. Ou the National Outstanding Young Scholarship in 2016.

Abstract:

Despite the extensive knowledge regarding the role of loss-of-function proteins in disease pathogenesis, our understanding of the cellular regulation of proteins in their hyperactive conformation remains limited. Here, I address how a cell governs hyperactive ciliary proteins. We have recently shown that RNA editing restricts hyperactive ciliary kinases by editing the kinase message RNAs, thereby reducing kinase production (Li et al., Science, 2021). Additionally, we have discovered that sensory neurons eliminate a de-repressed form of an intraflagellar transport (IFT) kinesin by directing it to neighboring glial cells for degradation. Through a combination of genetic suppressor screens and single-molecule assays, we provide compelling evidence that the conformation and activity of the kinesin dictate its fate. These findings highlight the remarkable ability of living cells to respond to hyperactive proteins through unexpected and diverse pathways, where distinct amino acid residues play a pivotal role in triggering specific cellular responses. Thus, we combine chemical mutagenesis and bioinformatics to systematically define functional residues essential for ciliary structure and function.

Maintenance of Lysosome Integrity and Function in C. elegans

Xiaochen WANG

Institute of Biophysics, Chinese Academy of Sciences

Biography:

Professor Xiaochen Wang got her PhD degree in the College of Life Sciences, Peking University in 1999 and accomplished her postdoc training at the University of Colorado, Boulder, USA in 2006. Dr. Wang started her laboratory at the National Institute of Biological Sciences (NIBS, Beijing) in 2006 and was promoted to an associate investigator at NIBS in 2011. She moved to the Institute of Biophysics, Chinese Academy of Science as a senior principal investigator in 2016. Dr. Wang was selected as the international early career scientist of Howard Hughes Medical Institute in 2012 and was awarded the 10th Young Female Scientist and the Distinguished Young Scholars Scientist in 2013. Her laboratory investigates lysosome hemostasis and lysosome-dependent clearance of apoptotic cells using *C. elegans* as a model system.

Abstract:

Lysosomes are membrane-bound acidic organelles that degrade macromolecules delivered by endocytic, autophagic and phagocytic pathways, and recycle metabolites to maintain cellular homeostasis. Lysosomes also serve as signal hubs that are critical for energy and amino acid sensing, signal transduction and autophagy regulation. We utilize *C. elegans* a multicellular model to investigate regulation of lysosome homeostasis and lysosome-dependent cellular degradation processes including clearance of apoptotic cells produced by programed cell death during development, and removal of residual body generated during spermatogenesis. We observed that lysosomes undergo a variety of dynamic changes in *C. elegans*, which associate with larval development, adult aging and stress conditions. By developing and employing *C. elegans* as a multicellular genetic model for a systematic investigation of lysosome homeostasis, we aim to identify signals/cellular processes that trigger/involve such lysosomal changes, dissect underlying regulatory mechanisms and reveal the physiological significance. In this meeting, I will present our work on lysosome function and regulation in *C. elegans* development and aging.

Understanding Metabolic Damage of Mitochondria

Chonglin YANG

Yunnan University

Biography:

Chonglin Yang received his PhD in Peking University in 1998, and finished postdoctoral training with Ding Xue in the University of Colorado, Boulder in 2005. From 2005 to 2016, he was an investigator in the Institute of Genetics and Developmental Biology (IGDB), Chinese Academy of Sciences (CAS). Since Oct. 2016, he has been a professor and Dean of the School of Life Sciences, Yunnan University, China. The Yang lab uses *Caenorhabditis elegans* as a multicellular model to dissect the mechanisms that govern the homeostatic maintenance of mitochondria and lysosomes.

Abstract:

Mitochondria are central to cell metabolism by coordinating multiple catabolic and anabolic pathways and coupling the tricarboxylic acid cycle with ATP production. Mitochondria dynamically interact with other organelles, and undergo constant fusion and fission, thus homeostatically maintaining their normal functions. However, the mechanisms that regulate mitochondrial homeostasis are not well understood. We aim to explore the effects of metabolism on mitochondrial homeostasis and to elucidate the underlying mechanisms by taking advantage of the unique *C. elegans*-based *in vivo* system. This talk will focus on our recent findings on how metabolic intermediates in mitochondrial oxidation of lysine and propionate cause mitochondrial damage and the implications in corresponding genetic disorders.

How Cell Stabilizes Endosomal F-actin?

Anbing SHI

Huazhong University of Science and Technology

Biography:

Dr. Shi is currently appointed as the Associate Dean of the School of Basic Medicine and the Dean of the Department of Biochemistry and Molecular Biology, Huazhong University of Science and Technology. Dr. Shi graduated from the School of Life Sciences, Nankai University, obtained his PhD degree in Cell Biology from Rutgers University (New Jersey, USA) and finished his postdoctoral training at Stanford University (California, USA). In 2012, Dr. Shi joined Huazhong University of Science and Technology as a faculty member, working on membrane trafficking regulation. Thus far, the research results have been published in peer-review journals, including *JCB*, *EMBO J*, *PNAS*, *PloS Genet*. Dr. Shi is currently a member of the Membrane Biology Branch of the Chinese Biophysical Society and Chinese Cell Biology Society.

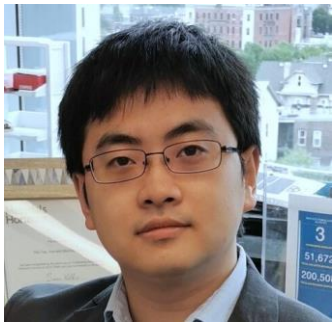
Abstract:

Cargo sorting and the subsequent membrane carrier formation require a properly organized endosomal actin network. To better understand the actin dynamics during endocytic recycling, we performed a genetic screen in *C. elegans* and identified RTKN-1/Rhotekin as a requisite to sustain endosome-associated actin integrity. Loss of RTKN-1 led to a prominent decrease in actin structures and the basolateral recycling defects. Furthermore, we showed that the presence of RTKN-1 thwarts the actin disassembly competence of UNC-60A/cofilin. Consistently, in RTKN-1-deficient cells, UNC-60A knockdown replenished actin structures and alleviated the recycling defects. Notably, an intramolecular interaction within RTKN-1 could mediate the formation of oligomers. Overexpression of an RTKN-1 mutant form that lacks self-binding capacity failed to restore actin structures and recycling flow in rtkn-1 mutants. Finally, we demonstrated that SDPN-1/Syndapin acts to direct the recycling endosomal dwelling of RTKN-1 and promote actin integrity there. Taken together, these findings consolidated the role of SDPN-1 in organizing the endosomal actin network architecture and introduced RTKN-1 as a novel regulatory protein involved in this process.

Session THREE
Development of Smart Therapeutics and Drug Delivery Systems

Session Chairs: Ruibing WANG and Ying ZHENG

Nano-/Microscale Materials-enabled Drug Delivery Technologies



Wei TAO

Harvard University

Biography:

Prof. Wei Tao is the Farokhzad Family Distinguished Chair for Innovation and Principal Investigator in the Center for Nanomedicine, Faculty Member in the Department of Anesthesiology, Perioperative, and Pain Medicine, and Faculty Member in the Gillian Reny Stepping Strong Center for Trauma Innovation at Brigham and Women's Hospital, Harvard Medical School. He is also the first Chaired Professor as an assistant professor in the history of his institution. He has published over 100 papers in prestigious journals including *Nature/Science/Cell Press/PNAS* family journals, and he is a Clarivate's Global Highly Cited Researcher (continuously selected since 2021). Prof. Tao's research interests include biomaterials, nanotechnology and drug delivery, as well as their various applications in translational medicine. Prof. Tao has received multiple awards/grants including the U.S. METAvivor Early Career Investigator Award, HMS/BWH Anaesthesia Department Basic Scientist Grant, Khoury Innovation Award, Center for Nanomedicine Research Fund, Stepping Strong Breakthrough Innovator Award, American Heart Association (AHA) Collaborative Sciences Award, MIT Technology Review Top Chinese Innovators Under 35 (2020 TR35), World's Top 2% Scientist (continuously selected since 2019), Chemical Society Reviews Emerging Investigator Award, Advanced Materials Rising Star, Materials Today Rising Star Award, Angewandte Chemie Most Outstanding Referees Award, Materials Horizons Top 10 Outstanding Reviewers Award, Nanoscale Emerging Investigator Award, Precision Nanomedicine Rising Talents Award, etc. He also serves on numerous editorial boards including as Founding Editor-in-Chief of Biomedical Technology (*Elsevier, KeAi's new journal*), Deputy Editor of Exploration (*Wiley's new journal*), and Associate Editor of Journal of Nanobiotechnology (*Springer Nature & BMC*); Guest Editor of eLife, etc.; Editorial Board Member of Bioactive Materials (*Elsevier, KeAi*), Nano-Micro Letters (*Springer Nature*), etc.; and Advisory Board Member of Matter (*Cell Press*).

Abstract:

Despite all of the coverage of new drugs, it is not enough to just have an effective drug. To enhance therapeutic efficacy and reduce the side effects, the drugs have to be protected and transported to the right location to get an effect at the right time. Over the past few decades, nano-/microscale materials-enabled drug delivery platforms have made tremendous advancements in preventing and treating human diseases. Especially, the recent great success achieved by the two highly effective mRNA nanoparticle vaccines during the COVID-19 pandemic further highlights the great potential of drug delivery technologies. During the evolution of these drug delivery technologies, materials science innovation has played an important role from drug modification to the synthesis of different drug delivery platforms, which fulfill effective medical applications in various diseases including cancers, cardiovascular diseases, diabetes, infectious diseases, and many others. In this talk, I will introduce our current studies on nano-/microscale materials-enabled drug delivery technologies with the promise to improve health care, as well as our efforts in accelerating their translation into the drug development pipeline.

Bacteria-based Therapeutics

Jinyao LIU

Shanghai Jiao Tong University

Biography:

Jinyao Liu is Professor and Assistant to the Dean of Institute of Molecular Medicine, Shanghai Jiao Tong University, China. After received his PhD at Shanghai Jiao Tong University in Materials Science and Engineering under the supervision of Prof. Deyue Yan in 2013, Jinyao joined Prof. Ashutosh Chilkoti's group in the Department of Biomedical Engineering at Duke University (04. 2013-08. 2015) and Prof. Robert Langer's laboratory in the Koch Institute for Integrative Cancer Research at MIT (09. 2015-03. 2018) as a postdoc associate. He is the associate editor of Journal of Nanobiotechnology (Springer Nature) and guest editor of Advanced Drug Delivery Reviews. His current research interests include bacterial-based bioagents, oral delivery, hydrogels, and nanomedicine. As corresponding author, he has published over 50 papers during the past 5 years in *Nat Biomed Eng*, *Matter*, *Nat Commun* (5), *Sci Adv* (5), *Angew Chem Int Ed* (2), *Adv Mater* (6), etc. Jinyao was also awarded numerous prestigious grants and prizes, including the Young Thousand Talents Program of China, 2022 JNB Rising Star, 2019 CASNN Rising Star, etc.

Abstract:

The gut microbiota has been demonstrated to be an important regulator in human health. Disorders in the gut ecosystem have been implicated in various diseases, such as inflammatory bowel disease, diabetes, Alzheimer disease, and even cancers. Although fecal microbiota transplantation has demonstrated effective to positively modulate the gut microbiome, the implementation has been largely restricted by invasive operation and indeterminate composition, which inevitably result in low patient compliance and potential safety issues. Oral delivery of probiotic species to the gut microflora is an alternative to address these limitations. Unfortunately, environmental complexity and a continuous flow within the gastrointestinal tract result in low oral bioavailability and limited intestinal colonization. Surface modification of bacteria, which includes chemical conjugation and physical encapsulation, has been utilized to introduce exogenous functions that are naturally unachievable. Recently, my group has wrapped bacteria with various entire coatings to increase bacterial survival and colonization *in vivo* following administration. In this presentation, I'd love to share the methodologies we have developed for engineering functional coatings on bacterial surface and also discuss the applications of these coated bacteria for enhanced treatment.

Bioresponsive Drug Delivery

Zhen GU

Zhejiang University

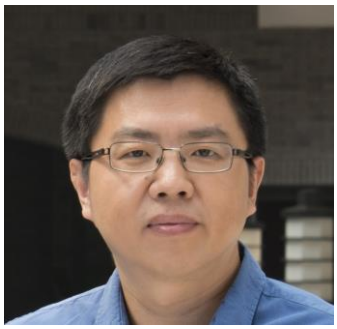
Biography:

Dr. Zhen Gu is a Qiushi Distinguished Chair Professor and Dean of College of Pharmaceutical Sciences at Zhejiang University. He also serves as the Director of the National Key Laboratory of Advanced Drug Delivery and Release Systems and Director of the Key Laboratory of Advanced Drug Delivery Systems of Zhejiang Province. Dr. Gu received his B.S. degree in Chemistry and M.S. degree in Polymer Chemistry and Physics from Nanjing University. In 2010, he obtained Ph.D. from the Department of Chemical and Biomolecular Engineering at the University of California, Los Angeles (UCLA). He was a Postdoctoral Associate working with Dr. Robert Langer at MIT and Harvard Medical School. Before he moved to Zhejiang University in 2020, he was a Full Professor in the Department of Bioengineering and Director of the NIH Biotechnology Training in Biomedical Sciences and Engineering Program at UCLA. From 2012 to 2018, he was working in the Joint Department of Biomedical Engineering at the University of North Carolina at Chapel Hill and North Carolina State University, where he was appointed as a Jackson Family Distinguished Chair Professor. Dr. Gu's group studies controlled drug delivery, biomaterials and cell therapy. He has published over 290 research papers and applied over 200 patents. He is a co-founder of five start-up companies, including Zenomics, ZCapsule and μZen. He is the recipient of the Felix Franks Medal of the Royal Society of Chemistry (2019), Young Investigator Award of CRS (2017), Sloan Research Fellowship (2016) and Pathway Award of the American Diabetes Association (ADA, 2015). MIT Technology Review listed him in 2015 as one of the top innovators under the age of 35 (TR35). He was elected to the College of Fellows of the American Institute for Medical and Biological Engineering (AIMBE) in 2019 and the International Academy of Medical and Biological Engineering (IAMBE) in 2021. Dr. Gu serves as an Associate Editor for Nano Research, Drug Delivery and Translational Research, and Regenerative Biomaterials. He also served as the CRS China Chapter President (2021-2022), Associate Editor for Science Advances (2019-2022).

Abstract:

Spurred by recent advances in materials chemistry, molecular pharmaceutics and nanobiotechnology, stimuli-responsive "smart" systems offer opportunities for precisely delivering drugs in dose-, spatial- and temporal-controlled manners. In this talk, I will discuss our ongoing efforts in developing physiological signal-triggered bioinspired drug delivery systems. I will first present the glucose-responsive synthetic systems for biomimetic delivery of insulin for diabetes treatment. Development of smart insulin patches will be emphasized. I will further discuss the local and targeted delivery of immunomodulatory therapeutics for enhanced cancer therapy. Our latest studies utilizing platelets, cell conjugates and sprayed gels for delivery of immune checkpoint inhibitors will be specifically introduced.

High Concentration Therapeutic Proteins: From Formulation Optimization To Protein Design



Feng QIAN

Tsinghua University

Biography:

Prof. Feng Qian is currently a professor and Dean of School of Pharmaceutical Sciences, Tsinghua University. Prof. Qian received his PhD in Biomedical Engineering from Case Western Reserve University, and his BS/MS from the Dept. Materials Science and Engineering, Tsinghua University, Beijing. Dr. Qian's current research interests include: 1). Novel therapeutics for pancreatic cancer and age-related macular degeneration, 2). Various drug delivery and formulation technologies to achieve optimized therapeutic or pharmaceutical benefits of existing drugs. Before joining Tsinghua in August 2012, Dr. Feng Qian held a position of Principal Scientist at Bristol-Myers Squibb Company from 2003 to 2012. Dr. Qian's research led to marketed drug products both in US and China. Prof. Qian is an author of over 70 peer reviewed papers, an inventor of over 10 patents/patent applications. Prof. Qian currently serves as an Associate Editor of Molecular Pharmaceutics.

Abstract:

Therapeutic protein with concentration over ~100mg/mL is often required for subcutaneous or intravitreal drug administration. In this talk, I will share our research journey, start from trial-and error type formulation optimization, all the way to design novel protein modality with intrinsic characteristics to obtain novel protein drugs with high potency, high concentration, low viscosity, and high stability.

Cutaneous Transport and Toxicity of Liposomal Doxorubixin: The Mechanisms and Clinical Interventions

Changyou ZHAN

Fudan University

Biography:

Dr. Changyou Zhan is a professor of pharmacology at School of Basic Medical Sciences, Fudan University. He obtained his Ph.D. in Pharmaceutics from Fudan University in 2010. His recent research focuses on understanding the in vivo delivery process of lipid-based therapeutics. Dr. Zhan has published >100 peer-review scientific papers with citation by >5600 times (H-index 43). His scientific achievements have been honored by scientific awards in China and the international, including, the National Outstanding Youth Funds of NSFC (2021), New Hundred-Talent Program of Shanghai Municipal Commission of Health and Family Planning (2018), Natural Science Award of MOE of China (2017), Natural Science Award of Shanghai City (2016), Postdoctoral Fellow Award of American Association of Pharmaceutical Scientists (2013) and National Outstanding Doctoral Dissertation Award of China (2012).

Abstract:

Liposomes are versatile drug delivery systems in clinical use for cancer and other diseases. Unfortunately, PEGylated liposomal doxorubicin (DOX-sLip) exhibits serious dose-limiting cutaneous toxicities (especially in skin and extremities) in clinical practice, which are closely related to the extravascular accumulation of DOX-sLip in dermis. No clinical interventions have been proposed for cutaneous toxicities due to the elusive transport pathways of liposomes. Herein, we showed that the reciprocal interaction between peripherally circulating neutrophils and liposomes played pivotal roles in liposomes extravasation into dermis. Neutrophils captured liposomes via the complement receptor 3 (CR3, CD11b/CD18) on cell membrane recognizing the fragment of complement component C3 (iC3b) adsorbed on the liposomal surface after complement activation. Liposomes also activated neutrophils to induce upregulation of membrane CD11b. Complement inhibitors, including CRIg-L-FH and glucocorticoids, could significantly reduce liposomes uptake by neutrophils and alleviate cutaneous accumulation of fluorescent probes or DOX encapsulated in liposomes. To further evaluate the effects of glucocorticoids on cutaneous toxicities of DOX-sLip in clinic, we analyzed the severity of hand-foot syndrome (HFS) in cancer patients receiving DOX-sLip, in which different doses of glucocorticoids were generally used to mitigate infusion reactions or as adjuvant therapy. Our data showed that glucocorticoids alleviated HFS in a dose-dependent manner in patients receiving DOX-sLip. These results provide potential solutions to the devastating cutaneous toxicities that occur during the treatment with DOX-sLip. Since cutaneous extravasation of other nanomedicines has been frequently reported, this mechanistic study also paves a new avenue to investigate the in vivo dynamic transport of particles.

Session FOUR
Cancer Research and Therapy Development

Session Chair: Kathy LUO

Contextual AI Approach of Classifying Earlier GI Tract Diseases

Hanry YU

National University of Singapore

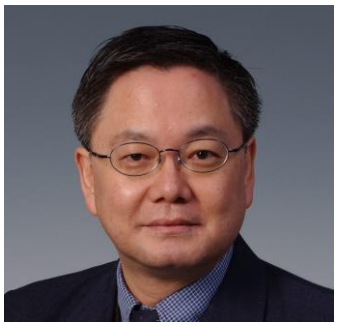
Biography:

Dr. Hanry Yu is a cell biologist by training, and ventured into many disciplines, partly because he enjoys being a student again and again. He has taught students in leading institutions in the US and Asia, built major programs in research and education, translated technologies into commercial products and services, and particularly enjoys mentoring many younger scientists and engineers in their journeys. He wants to be philosophical in doing science and scientific in doing engineering.

Abstract:

Early diagnosis of ulcerative GI tract diseases and colorectal cancer by endoscopy is important but challenging. AI based approach is promising but suffers from the limited clinical training dataset sizes typically available (hundreds-thousand). To maximise the extraction of relevant information, we have developed a contextual framework in which both lesions and contexts are separated and preserved for differential treatments and weight-integrated in building classifiers. The contexts are both at tissue-object or image level, and at spatial or patient level. This framework enables extremely high accuracy of predicting colorectal cancer invasion depth and multi-class classification of benign ulcerative diseases to identify and treat early diseases that likely would progress further, during endoscopic screening.

Phytochemicals Regulate Angiogenic Functions in Endothelial Cells by Binding to Vascular Endothelial Growth Factor (VEGF): Drug Development Targeting to Cancer Therapy



Karl TSIM

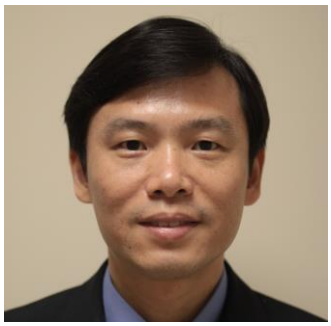
The Hong Kong University of Science and Technology

Biography:

Prof. Karl Tsim received his BSc and MPhil from The Chinese University of Hong Kong, and PhD in Molecular Neurobiology from the University of Cambridge, UK. After his post-doctoral training at Stanford University, USA, he joined The Hong Kong University of Science and Technology (HKUST) in 1992. Currently, he is a Chair Professor of Division of Life Science, Director of Center for Chinese Medicine and Director of Shenzhen Key Laboratory of Edible & Medicinal Bioresources at the university. He is the Founding Chairman of Hong Kong Association of Biotechnology in Chinese Medicine. Prof. Tsim has developed molecular technique to determine the genetic and chemical properties of Chinese herbs. He has published about 500 scientific papers and serves as editors for many scientific journals internationally. His works on Chinese herbal medicine have been awarded twice for Research Excellence in *Natural Sciences* from Ministry of Education of China. He also serves as an adviser/consultant/member to various organizations, both nationally and internationally, in the standardization of Chinese herbs, which include WHO and HKSAR Government in Testing and Certification of Chinese herbs. He is an active entrepreneur and is the founding director of few companies.

Abstract:

To identify active phytochemicals from traditional Chinese medicine (TCM) for drug development, a microarray-based drug screening platform, constructed by arraying HPLC fractions of herbal extracts onto a surface-activated polystyrene slide, has been developed, named as “HerboChips” The biotinylated-vascular endothelial growth factor (VEGF) was hybridized with the chips coated with different HPLC-separated fractions from the herbal extracts. By screening over hundreds of herbal extracts, positive hits were identified. The binding interaction of identified phytochemicals with VEGF was further confirmed both *in vitro* and *in vivo* studies, i.e., the phytochemicals could exert effects on VEGF-induced cell proliferation and cell migration. In human umbilical vein endothelial cells (HUVECs), the application of the phytochemicals suppressed the angiogenic functions of VEGF, which were illustrated to interact with VEGF at VEGF receptor 2 (VEGFR2) binding site, and thereafter reducing the receptor signalling cascade, including activations of phosphorylated VEGFR2, phosphorylated eNOS, and phosphorylated ERK 1/2. These identified phytochemicals by binding to VEGF could be developed into herbal/drug products for anti-tumour therapy, as well as the treatment of age-related macular degeneration (AMD) disease. The current results supported the applicability of natural products from TCM in VEGF-mediated diseases.



Imaging Guided Multimodal Cancer Therapy Based on Nano-Multizymes

Peng CHEN

Nanyang Technological University

Biography:

Dr. Peng Chen obtained his bachelor degree from Zhejiang University (China) and obtained his PhD degree at University of Missouri, Columbia (US) where he conducted research on single cell analysis to study exocytosis. During his post-doctoral training at Harvard University (US), he conducted research on nanopore-based DNA sequencing. In 2005, he joined School of Chemical & Biomedical Engineering at Nanyang Technological University as an assistant professor. Currently he is a full professor in the School of Chemistry, Chemical Engineering and Biotechnology, Lee Kong Chian School of Medicine, Institute for Digital Molecular Analytics and Science at Nanyang Technological University, and also the chief engineering for Skin Research Institute of Singapore. He is a fellow of Royal Society of Chemistry and a global highly cited researcher (Clarivate). His current research interest mainly focuses on theranostic technologies and nanomaterials.

Abstract:

Nanozymes are inorganic nanoparticles that display enzyme-mimetic activities. They often outperform natural enzymes because of excellent stability, high catalytic activity, multifunctionality and low cost. In this presentation, I would like to demonstrate some rationally designed multi-functional nanozymes, which simultaneously possess multiple nanocatalytic abilities and other useful physiochemical properties (e.g., photothermal and ferromagnetic effects). Further, imaging (photoacoustic or magnetic resonance) guided, synergistic multimodal (chemodynamic / photodynamic / photothermal) cancer therapy with high efficiency, good specificity, and low side effects are demonstrated.

Co-cultured Spheroids as Model Systems for Tumour Micro-environment and Drug Testing

G. J. (FRITS) PETERS

Amsterdam University Medical Centers

Biography:

The research of Prof. Peters is focused on translation of preclinical pharmacology of anticancer agents to the clinic, and on drug development (from screening to Phase I and II trials) of anti-signalling protein kinase inhibitors, antifolates, antimetabolites, platinum analogs, topoisomerase inhibitors, and taxanes. The focus is on drug combinations, proper prodrugs or drug carriers and identification of resistance genes as biomarkers to select the proper drug for personalized therapy. Other research interests include regulation of transport and metabolism, DNA repair, apoptosis and protein processing (proteasome, aminopeptidase, autophagy). These research fields are interconnected by studying the role of phosphorylation by various protein kinases on the function of these pumps and receptors. Prof Peters supervised more than 30 PhD and over 100 master students and guest scientists from all continents. He was chair of the examination committee of the Master Oncology. He has (co)-authored >700 refereed research papers and reviews (H-index 99), is/was member of >50 editorial boards, and initiated Cancer Drug Resistance.

Abstract:

Tumour microenvironment seems to play a key role in chemoresistance. Pancreatic stellate cells (PSCs), are part of the tumour and may have an important role in chemoresistance of pancreatic ductal adenocarcinoma (PDAC). We developed novel 3D spheroid models to evaluate the role of PSCs in drug resistance of primary human PDAC. PSCs may induce drug resistance in PDAC cells by paracrine secretion of growth promoting signaling molecules, such as hepatocyte growth factor (HGF), which may activate the c-MET pathway. These novel models were developed by growing together immortalized GFP-expressing PSCs and CFP-firefly luciferase(Fluc)-expressing PDAC cells. Cancer cell growth and drug response were examined by luciferase assay, while spheroids architecture was evaluated by confocal microscopy. Drug response was studied in five primary human PDAC cells growing as monolayers by sulforhodamine-B assays. PSCs-conditioned medium (PCM) increased phospho-c-MET expression which was highest in PDAC5 cells and the subclone PDAC5(SSEA4). Remarkably, PCM of cells pre-incubated with PDAC-conditioned medium, which contained increased HGF levels, made PDAC5 and PDAC5(SSEA4) cells significantly more resistant to gemcitabine, but not to c-MET inhibitors. The presence of PSCs in PSC/PDAC5(SSEA4) hetero-spheroids induced significant cancer cell growth and gemcitabine resistance compared to PDAC-homo-spheroids. However, c-MET inhibitors such as tivantinib, PHA-665752 and crizotinib were equally effective in homo- and hetero-spheroids. Primary human PSCs experiments confirmed the main findings. In conclusion, we developed spheroid models to evaluate the reciprocal interaction of PSCs and primary PDAC cells. These new models, which could be used for pharmacological evaluation of different drug candidates in a biologically relevant context, showed that PDAC cells are highly resistant to gemcitabine in the presence of PSCs, but c-MET inhibitors could overcome this chemoresistance.

Elucidating How Circulating Tumour Cells Resist Fluidic Shear Stress in Circulation and Acquire Stronger Metastatic Capacities

Kathy LUO

Biography:

Kathy Qian Luo is a Professor and Associate Head of the Department of Biomedical Sciences in the Faculty of Health Sciences, University of Macau (UM). Prof. Luo received her BS and MS degrees from Peking University and Ph.D. degree from the University of British Columbia in Canada. Before joining UM, she has worked in California Institute of Technology in USA, Hong Kong University of Science and Technology, and Nanyang Technological University in Singapore. Prof. Luo's research areas include circulating tumour cells, cancer metastasis, anti-cancer drug development, and study of cell death in sensor zebrafish. Prof. Luo has published 96 papers in many top tire journals including *Science Advances*, *Oncogene*, *Biosensors and Bioelectronics*, which have been cited for 6,591 times. She has obtained 7 patents from USA, China and Singapore. She has received 35 research grants with a total funding of MOP98 million (US$12 million). She has supervised 9 Postdocs, 31 Ph.D. students, 24 M.S. students, and 9 RAs.

Abstract:

Circulating tumour cells (CTCs) are the major source of metastatic tumours, which cause 90% of cancer-associated deaths. Thus, understanding how CTCs can survive in circulation is crucial for designing new therapies to prevent metastasis and increase the survival of cancer patients. To study how cancer cells can withstand fluid shear stress (SS), Prof. Luo's research team has developed a microfluidic circulatory system and used it to isolate SS-resistant breast and lung cancer cells. These SS-resistant cells showed higher abilities to form clusters, survive in circulation, and metastasize in mice. Detailed analyses showed that these cells expressed 4-5-fold more desmocollin-2 (DSC2) and plakophilin-1 (PKP1) proteins, which facilitated cancer cells to form clusters in circulation, and also activated PI3K/AKT/Bcl-2–mediated pathway to increase cell survival. The high levels of DSC2 and PKP1 are also important for maintaining high expression of vimentin, which stimulates fibronectin/integrin β1/FAK/Src/MEK/ERK/ZEB1– mediated metastasis. Moreover, higher levels of DSC2 and PKP1 were detected in tumour samples from patients with breast and lung cancer, and their high expression was correlated with lower overall survival and worse disease progression. Therefore, DSC2 and PKP1 may serve as new biomarkers for detecting and targeting metastatic circulating tumour cells. This work has been published in *Science Advances*, 2021, 7 (40) eabg7265 under the authors of Koukou Li, Renfei Wu, Muya Zhou, Haibo Tong and Kathy Qian Luo from the Faculty of Health Sciences, University of Macau.

Session FIVE
Biology of Aging

Session Chair: Wakam CHANG
Co-Chair: Garry WONG

Disorganized Chromatin Hierarchy Drives Stem Cells Aging in Atypical Laminopathy-based Progeria Mandibuloacral Dysplasia Type A

Zhongjun ZHOU

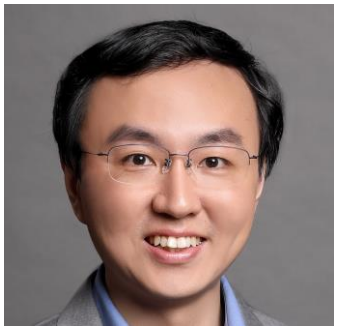
The University of Hong Kong

Biography:

Prof Zhongjun Zhou received his BSc degree from Xiamen University, and PhD degrees from Chinese Academy of Medical Sciences & Peking Union Medical College (1993) and from Karolinska Institute, SWEDEN (2004). His research focuses on understanding the mechanisms of aging, particularly the regulation of chromatin remodeling and DNA repair as well as stem cell renewal. He is also interested in growth factor signaling regulated by extracellular matrix and proteinases. His major contribution to the scientific community is to have identified several signaling pathways regulated by specific metalloproteinase and extracellular matrix components during development and aging, providing insightful mechanistic explanations for several human developmental defects and diseases. He is the one to first propose genomic instability in Hutchinson-Gilford Progeria syndrome and has elucidated the epigenetic disturbance that accelerates the aging processes in HGPS patients. In addition, his work has revealed the underlying mechanism for SIRT6 in human longevity and aging. Prof Zhou received several awards for his significant contribution to the fields including the Distinguished Overseas Young Chinese Scholar Award (2006) from Natural Science Foundation of CHINA, the Outstanding Research Award of University of Hong Kong (2014) and Croucher Senior Research Fellow (2015). Prof Zhou is the associate editor of journal "*Mutation Research*" and Editor-in-Chief of "*Translational Medicine of Aging*", academic editor for "*Aging Cell*". He is the founding Chairman of Asian Society of Aging Research. He is also the elected Chairman of Hong Society of Cell Biology and Founding president of Asian Society of Aging Research.

Abstract:

The studies of laminopathy-based progeria provide insights into aging and aging-associated diseases and uncover the function of lamins in chromatin organization and remodeling. Mandibuloacral dysplasia type A (MAD) represents largely unexplored atypical progeria without defect in prelamin A post-translational processing. Using MAD patient-specific iPSCs carrying homozygous LMNA p.R527C, premature aging phenotypes were recapitulated in multiple mesenchymal lineages, including mesenchymal stem cells (MSCs). Comparative analysis of the transcriptome across 26 aging human MSCs (hMSCs) models found that MAD-MSCs share the highest similarity with senescent primary hMSCs. Analysis of lamina-chromatin interaction revealed that both the reorganization of lamina-associating domains (LADs) and repositioning of non-LAD binding peaks facilitate accelerated senescence. Investigation of 3D genome organization further supported the contribution of MAD mutation to disorganized chromatin hierarchy, leading to dysregulation in epigenetic modifications, stem cell fate maintenance, senescence, and geroprotection. These results altogether demonstrate that LMNA missense mutation drives cellular senescence, leading to accelerated aging-associated pathogenesis by altering multidimensional chromatin architecture in an atypical progeroid syndrome.



The Trigger of the Germline Longevity

Yidong SHEN

Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences

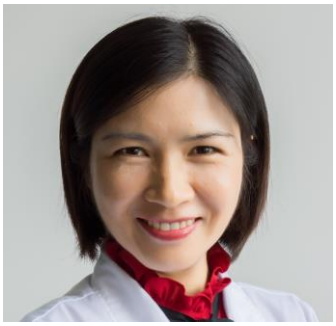
Biography:

Dr. Shen received his PhD from Shanghai Institute of Biochemistry and Cell Biology, CAS, in 2008. He performed his postdoctoral research in Adam Antebi lab, Max Planck Institute for Biology of Ageing, with the EMBO Long-Term Fellowship and CECAD senior postdoc fellowship. Dr. Shen became a professor, group leader, and principal investigator at Shanghai Institute of Biochemistry and Cell Biology, CAS since his return to China in 2014, supported by the Thousand Talent Program for Young Outstanding Scientists.

Abstract:

Reproduction and aging are closely linked. The absence of germline significantly extends the lifespan in various animals. Yet, how the reproductive system senses the loss of germline and subsequently triggers longevity is poorly understood. In this talk, I will present our recent findings in nematode *C. elegans* that the distal tip cell (DTC), the niche of germline stem cells (GSCs) is critical in inducing germline longevity. Our studies thus highlight the stem cell niche-derived signaling in aging.

Telomere Stability Regulation and Cellular Senescence



Haiying LIU

Sun Yat-Sen University

Biography:

Haiying Liu graduated from Tsinghua University, and now is an associate professor of Sun Yat-Sen University. Her lab mainly focuses on telomere stability and senescence the mechanisms of telomere stability maintenance.

Abstract:

Telomere is an important protective structure at the end of linear chromosomes. Extremely short telomeres trigger cellular senescence in normal cells. We found that the cytosolic DNA sensor cGAS binds to short telomeres and protects them from end-to-end fusion in metaphase. In human primary cells, deletion of cGAS leads to short telomere fusion and failure of replicative senescence. Besides short telomeres, telomere transcription and its product TERRA also regulates telomere stability. TERRA forms R-loops at telomeres and plays as a double-edged sword to telomere stability. We found that TCOF1 regulates telomere transcription and METTL3 regulates the stability of TERRA, knocking down either of which leads to telomere instability in cancer cells.

Session SIX
Drug Discovery and Biomaterials for Immune Regulation

Session Chairs: Yunlu DAI and Joong Sup SHIM

Discovery of Small Molecules for Tumour Immuno-Regulation

Yongjun DANG

Chongqing Medical University

Biography:

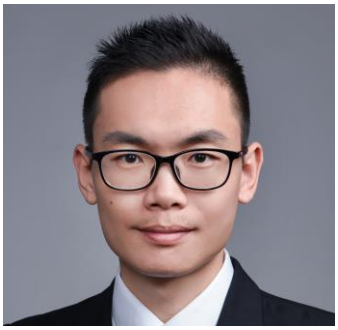
Yongjun Dang is the Professor and Director of Center for Novel Target & Therapeutic Intervention at Chongqing Medical University. He mainly engages in disease-related targets and small molecule discovery, confirmation, and translational medical research, which besides:

1. molecular target identification and mechanism research of natural products;
2. biological research based on small molecule probes;
3. establishment of models for therapeutic intervention-related high-throughput screening.

In the past five years, he has published 17 papers in well-known journals such as Signal Transduct Target Ther, Angew Chem Int Ed, Adv Sci, Protein Cell, and J Clin Investig as the corresponding author. His articles have been cited more than 5,200 times, with an H-index of 32.

Abstract:

Immune response plays an important role in anti-tumour immunity, but tumours usual evade the attack of immune system by limiting the recognition and activity of immune cells. We constructed high-throughput screening system to discovery anti-tumour small molecules which could regulate the tumour immunity, and found L-5HTP specifically inhibited the IFN-γ-induced PD-L1 expression and activated the T-cell anti-tumour effect. Alisertib upregulated PD-L1 expression and increased the T cells infiltration, which improved the efficacy of PD-L1 blockade therapy. The platinoid compound Bis(benzonitrile) dichloroplatinum (II) can destroy the PD-1/PD-L1 interaction and enhance the T-cell cytotoxicity activity. Our research provides powerful tool to discovery the leading compounds that potentially affect tumour immunity.



Proteostasis and Antitumour Immunity

Liang CHEN

Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences

Biography:

Prof. Chen finished his PhD training during 2008-2014, graduate from Cell Biology, College of Life Science, Peking University；2014-2018 did post-doctoral research at Tumor Biology, School of Medicine, University of Pennsylvania. 2018.07 to today, work as an Associate Professor for Shenzhen Institute of Advanced Technology (SIAT), Chinese Academy of Sciences. And also became a member of "Overseas High-level Talents of Shenzhen" at 2018. Prof. Chen's team has long been working on targeted protein degradation for cancer targeted therapy and also anti-tumor immunity. The Chen-lab used targeted protein degradation approach and discovered several novel actionable targets for major types of cancer. These studies have been published in several prestigious journals, including *J. Am. Chem. Soc.* (2022), *Nat Commun* (2018 and 2020), *J Exp Clin Canc Res* (2022), *Cell Rep* (2017), and *Clin Transl Med* (2021, and 2022).

Abstract:

TBC

Dynamic Nano-Assemblies-based Biomaterials and Drug Delivery Systems

Daishun LING

Shanghai Jiao Tong University

Biography:

Prof. Daishun Ling received his Ph.D (2012) in School of Chemical and Biological Engineering, Seoul National University. Later, he worked as a professor in the College of Pharmaceutical Sciences, Zhejiang University. Now, he is a distinguished professor in Frontiers Science Center for Transformative Molecules, School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University. Prof. Ling's primary research interest has been focusing on the assembly/disassembly chemistry, stimuli-responsive biomaterials, dynamic nanoassembly based drug delivery systems. Up to now, he has published 142 papers (with over 12000 citations) in prominent international journals including *Nature Nanotechnol*., *Nature Mater*., *Nature Biomed. Eng., Nature Commun., J. Am. Chem. Soc., Angew. Chem. Int. Ed., Adv. Mater., Adv. Sci., Natl. Sci. Rev., Adv. Funct. Mater., Nano Today, ACS Nano, Nano Lett., ACS Cent. Sci.,* etc. He has been serving as the Associate Editor of *Exploration*, Assistant Editor of *J. Control Release*, Theme Editor of *Adv. Drug Deliv. Rev*., Academic Editor of The Innovation, and the Editorial Board Member of *Sci. Bull*. He received the "Journal of Nanobiotechnology Rising Star Award" (2021), Best Reviewer Award of Science Bulletin (2020), National Science Found for Excellent Youth Scholars (2019), First prize of Science and Technology Progress Award of Ministry of Education (2018), Second prize of Science and Technology award of Zhejiang Pharmaceutical Association (2018).

Abstract:

Nanotechnology has received extraordinary attention recently due to its important role in biomedical research. The materials composing the nanoparticles produce fascinating and diverse functionalities. The controllable assembly mediated by a multitude of different ligands would lead to the flexible modulation of nanomaterials' fate *in vivo*, endowing the nanoplatform with targeted delivery and accumulation to disease lesions. The clever fabrication of dynamic nanoparticle assemblies via the ligands directed nanoparticle self-assemblies would lead to developing multifunctional nano-biomedical platforms for simultaneous targeted delivery, fast diagnosis, and efficient therapy. Furthermore, the ingenious control over the assembly/disassembly process based on small-sized inorganic nanoparticles could achieve both *in vivo* targeted delivery and environmental stimuli-responsive disassembly for efficient disease therapy and bioelimination. Overall, dynamic nano-assemblies based biomaterials and drug delivery systems can achieve the improved diagnostic accuracy and therapeutic efficacy in many diseases including cancer, infection and neurodegenerative diseases.

Smart Nanomedicine for Cancer Immunotherapy

Haijun YU

Shanghai Institute of Materia Medica, Chinese Academy of Sciences

Biography:

Prof. Haijun Yu is a professor and principal investigator in Shanghai Institute of Materia Medica, Chinese Academy of Sciences. His group is devoted to developing novel drug delivery systems and clinical translation for cancer immunotherapy. His group has developed a set of stimuli-activatable and prodrug-based drug delivery systems with improved drug delivery efficacy and therapeutic performance.

Abstract:

Immunotherapy has emerged as a promising clinical modality for cancer therapy due to its ability to initiate an antitumour immune response. However, current immunotherapy is severely impaired by immunosuppression of host T-cell antitumour activity through the programmed cell death 1 ligand (PD-L1) and programmed cell death receptor 1 (PD-1) (PD-L1/PD-1) immune checkpoint or IDO-1. For instance, we had developed a tumour acidity and reduction microenvironment dual-activatable binary cooperative prodrug nanoparticle (termed as BCPN) for immunotherapy (Figure 1). BCPN was prepared by self-assemble of a polyethylene glycol (PEG)-grafted OXA prodrug and a disulfide bond-crosslinked homodimer of NLG919. In comparison of the previously reported nanovectors, BCPN is of several unique advantages for cancer immunotherapy. First, BCPN displays high drug encapsulation efficacy and tunable drug loading ratios by simply adjusting the feeding ratios of two prodrugs. Second, the PEGylated OXA prodrug is of superior sensitivity to the extracellular acidic pH of tumour. Upon reaching the tumour acidic microenvironment, BCPN switches to a positive surface charge following cleavage of the PEG corona, thereby improving tumour penetration and cellular uptake. The OXA prodrug and NLG919 dimer can be activated in the reduction microenvironment of tumour cells to avoid side effects.

3D Printing of Biomimetic Biomaterials and Cells

Chengtie WU

Shanghai Institute of Ceramics, Chinese Academy of Sciences

Biography:

Prof. Chengtie Wu is from Shanghai Institute of Ceramics, Chinese Academy of Sciences (SIC, CAS), and He is the Outstanding Youth of NSFC, the Principal Investigator for National Key Research and Development Program of China. Prof Wu's research focuses on bioactive inorganic materials for tissue regeneration. He completed his Ph.D in 2006, and then he worked in the University of Sydney, Dresden University of Technology, Germany and Queensland University of Technology where he was awarded Vice-Chancellor Research Fellow and Alexander von Humboldt Fellow. In 2012, Dr Wu has been recruited to work in SIC, CAS, as Leading Talent Program of Chinese Academy of Sciences. Then he was awarded Recruitment Program of Global Young Experts of China, National Ten Thousand Plan Science and Technology Leader, Shanghai Pujiang Talent Program and Shanghai Outstanding Academic Leaders. Up to now, Prof Wu has published more than 280 SCI peer-review journal papers, including Science Advances, Advanced Materials, Materials Today, ACS Nano, Biomaterials and Nano Letters, etc. From 2015 to 2022, the applicant was honored by "Most Cited Chinese Researchers" for eight consecutive years, which was issued by *Elsevier* publisher, H index: 84. He is now the Associate editors for "*Applied Materials Today*" and "*Journal of Inorganic Materials*"as well as the editorial board member of "*Acta Biomaterialia*"and "*Bioactive Materials*" Prof Wu has been awarded 60 patents, in which 18 of them have been transferred to companies. Prof Wu was awarded the Journal of Materials Chemistry Lectureship in 2015, Young Scientists of Chinese Biomaterials Society in 2016, Outstanding Young Scientists of Chinese Ceramics Society in 2018, First Prize of Science and Technology of Chinese Biomaterials Society in 2019, and Second Prize of Science and Technology of Jiangsu Province in 2020.

Abstract:

3D printing technology is one of the most promising technologies in the field of tissue engineering and regenerative medicine. It can stack multiple components (materials, cells, etc.) layer by layer in three-dimensional space, thereby constructing complex and accurate structures. The 3D printing method has far surpassed other traditional manufacturing methods for the construction of tissue regeneration scaffolds. How to construct personalized tissue regeneration scaffolds with different compositions, structures, and functions through ingenious design and 3D printing technology is a research focus in the field of regenerative medicine. We have carried out a series of research work aimed at the needs of 3D printing scaffolds for biomimetic and functional purposes, from material design, structural regulation, to functional modification, to multicellular printing of artificial tissue, and developed a variety of 3D printing tissue regeneration scaffolds with excellent biological functions. Firstly, we have constructed a series of bionic scaffolds with excellent tissue repair performance by regulating the macro/micro structure of 3D printing scaffolds. Macroscopically, through precise model design, printing out scaffolds such as bionic lotus root and natural bone multi-level structure can effectively promote vascularized bone regeneration. On the micro level, by combining microbial catalysis and other technologies with 3D printing technology, a 3D printing scaffold with specific micro and nano structures has been constructed, significantly improving the osteogenic performance of the scaffolds. The scaffolds with a single repair function cannot achieve ideal therapeutic goals for tissue defects caused by diseases. Therefore, we further combined 3D printing technology with surface modification strategies to develop a variety of 3D printing scaffolds that have dual functions of tumour treatment and tissue regeneration, thereby more effectively curing defects caused by tumour diseases. In addition, for the regeneration and construction of complex tissues/organs, it is necessary to develop biomimetic scaffolds with multiple cells arranged regularly. Then, we further extend 3D material printing to 3D multicellular printing, by regulating the composition of biological ink, designing the spatial distribution of cells, and constructing multicellular scaffolds that simulate different complex tissues. Multicellular scaffolds constructed through 3D cell printing have excellent tissue regeneration functions *in vivo* and *in vitro*, which offers a foundation for three-dimensional reconstruction of other complex tissues/organs.

Session SEVEN
Stem Cell, Gene and Cell Therapy

Session Chair: Guokai CHEN
Co-Chair: Ren-He XU

A Single-nucleus Survey of Mammalian Hibernation for Liver Protection

Ji DONG

Bioland Laboratory, Guangzhou

Biography:

Prof. Ji Dong achieved his PhD degree from Peking University and joined Guangzhou National Laboratory in 2020. His reseach interests mainly focus on developmental biology, tumour biology and single-cell omics. He is dedicated to utilize advanced technologies (e.g., single-cell omics, bioinformatics, organoid culture, gene editing etc.) to explore regenerative medicine related issues, including aging, cancer and torpor. His works have been published in *Cell Stem Cell*, *Cell Research*, *Genome Biology*, *Briefings in Bioinformatics*, etc.

Abstract:

During winter, mammalian hibernators lower body temperature and suppress metabolism to survive stressful conditions. However, how do hibernators protect their organs from hypothermia and ischemia-reperfusion remains elusive. Here, we used Myotis ricketti as a model to study its liver protection during hibernation. We sampled bat livers and profiled their single-nucleus transcriptomes at 5 time points, including torpor, 2, 6 and 24 hours after arousal, and active period. Several cell types and molecular clues were identified and validated to be crucial for liver protection during hibernation. In this symposium, I will share our new and exciting results, and hope these findings can provide unique insights to prevent organ damage in transplantation or ischemia-reperfusion.

Gene Editing Therapy of β-Thalassemia

Junjiu HUANG

Sun Yat-Sen University

Biography:

Vice Dean of School of Life Sciences, Sun Yat-sen University. He published the world's first report of human embryos altered by gene editing using CRISPR/Cas9 and was mention in "365 days: Nature's 10" in 2015. He also the first one corrected β -thalassemia point mutant by base editor in human embryos, which was mentioned in "2017 in news: The science events that shaped the year"in Nature.

Abstract:

With the completion of the Human Genome Project, the decoding of human genetic information promotes the diagnosis and treatment of diseases into the era of genomics. Many "rare diseases" and "incurable diseases" have also been gradually unveiled, and more and more diseases have been confirmed as genetic disorders. CRISPR/Cas gene editing technology which was discovered and applied in 2012 has been proved to be one of the most breakthroughs in the biomedical field in the past decade. With the characteristics of simplicity, high efficiency and a wide range of applicability, this technique has not only been widely used in the study of gene function, but also made important progress in clinical trials of gene therapies for genetic disorders. For monogenic disorders with clear genetic background, CRISPR/Cas based technology can change the endogenous gene sequence or re-regulating the gene function through editing the target DNA sequence precisely to cure this kind of genetic disorders. Herein, we would like to talk about the research progress of gene editing drugs in β-thalassemia.

Live-seq Enables Temporal Transcriptomic Recording of Single Cells

Wanze CHEN

Shenzhen Institute of Synthetic Biology and Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences

Biography:

Wanze Chen is a professor at Shenzhen Institute of Advanced Technology (SIAT), Chinese Academy of Sciences. Dr. Chen received his PhD from Xiamen University, China. He then studied in the Laboratory of Systems Biology and Genetics as a postdoc at EPFL in Switzerland before establishing his lab at SIAT. The research focus of his lab is to understand and program the fate of stem cells. Driven by this primary interest, they actively develop and utilize multidisciplinary technologies, such as live cell RNA-seq, genome-wide genetics perturbation, miniaturized large-scale functional screening, etc. The current projects include stem cell *in vitro* expansion, single-cell RNA-seq-assisted cell programming, and microfluidic-based large-scale phenotyping. The projects are well funded and currently recruiting talented students and postdocs.

Abstract:

Single-cell transcriptomics (scRNA-seq) has greatly advanced our ability to characterize cellular heterogeneity. However, scRNA-seq requires lysing cells, which impedes further molecular or functional analyses on the same cells. Here, we established Live-seq, a single-cell transcriptome profiling approach that preserves cell viability during RNA extraction using fluidic force microscopy, thus allowing to couple a cell's ground-state transcriptome to its downstream molecular or phenotypic behaviour. Live-seq has the potential to address a broad range of biological questions by transforming scRNA-seq from an end-point to a temporal analysis approach.

Understanding and Managing of Male Infertility Based on Mechanism Study

Xiao Yang ZHAO

Southern Medical University

Biography:

Dr. Zhao is the vice depute director the basic medical college. He was graduate from IOZ, CAS for PhD in 2011, and then set up the lab to study spermatogenesis and infertility. In the past 10 years, he had authored more than 50 SCI papers including *Nature, Cell Stem Cell, Nature protocols, Cell Research, JBC* and other journals.

Abstract:

Global rates of male infertility continuing to rise, which raising serious medical concern, though the mechanism remains poorly understood. Impaired male reproductive function affects approximately half of infertile couples worldwide. Recent years, our group utilized cutting-edge technologies that deeply interrogate the genome, transcriptome, and the epigenome, even at single-cell level, besides the breakthroughs in robotic surgery, investigated the mechanism of male infertility, and offer promises towards solving male factor infertility. Here we will introduce our recently progress in this area.

Session EIGHT
Cell Death

Session Chair: Hanming SHEN

Necroptosis on the Brake

Liming SUN

Institute of Biochemistry and Cell Biology and Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences

Biography:

Liming Sun is a professor at the Center for Excellence in Molecular Cell Science, Chinese Academy of Sciences. Her research is primarily concerned with the molecular mechanism of necroptosis signaling, and its relevance to human diseases. Her major scientific contributions include: (1) identified of MLKL as necroptosis executioner, which was activated by RIP3-mediated phosphorylation; (2) discovered MLKL inhibitor NSA, which targets hMLKL-Cys86; (3) developed monoclonal antibodies as necroptosis biomarkers that specifically recognizing p-RIP3 and p-MLKL; (4) characterized new mechanism of action of microtubule-targeting agents (MTAs) killing the adjacent tumour cells via membrane bound-TNF-mediated cell death; (5) identified necroptotic cell-releasing factor modulates stem cell niche to promote tissue repair; (6) identified necroptosis-inhibitory phosphorylation on MLKL.

Abstract:

Necroptosis is a form of newly defined programmed cell death. The fundamental characteristic of necroptotic cell death is the loss of membrane integrity and the release of intracellular contents. The necroptosis cell-released factors, so-called damage-associated molecular patterns (DAMPs), have drawn the most attention of researchers to study their pro-inflammatory roles in the past decades. Uncontrolled necroptosis leads to human diseases, such as rheumatoid arthritis and neurodegenerative diseases. Recently, we identified multi-levels of necroptosis-inhibitory regulations on the key necroptosis components RIP3 and MLKL, which explained how cells/organisms are protected from spontaneous necroptosis injury.

Cell Death-Dependent and -Independent Functions of RIPK1/RIPK3 in Inflammatory Diseases

Sudan HE

Suzhou Institute of Systems Medicine

Biography:

Dr. Sudan He is currently a Principal Investigator and Vice Director of the Institute of Systems Medicine, Chinese Academy of Medical Sciences & Peking Union Medical College. She received her PhD from Peking Union Medical College in 2008 and then conducted postdoctoral research at the National Institute of Biological Sciences in Beijing, in the lab of Prof. Xiaodong Wang where she studied the mechanism of programmed necrosis/necroptosis. Since December 2010, she established his own lab as a faculty member of the Cyrus Tang Hematology Center at Soochow University. In 2018, she joined the Chinese Academy of Medical Sciences & Peking Union Medical College as a Principal Investigator. Her research interests include the molecular mechanisms of cell death with particular emphasis on necroptosis and the roles of necroptosis in inflammatory diseases and cancer.

Abstract:

Necroptosis is a tightly regulated form of necrosis that requires the activation of receptor-interacting protein (RIP) kinases RIPK1 and RIPK3, as well as the RIPK3 substrate MLKL (mixed lineage kinase domain-like protein). Necroptotic cells release cellular contents including damage-associated molecular patterns (DAMPs) that evoke immune responses. Graft-versus-host disease (GVHD) is a life-threatening complication in patients undergoing allogeneic hematopoietic stem cell transplant (allo-HSCT), involving injury to host normal tissues caused by alloreactive donor T cells. Here, we demonstrate that intestinal epithelial cell (IEC) RIPK1/RIPK3 axis is crucial for triggering and amplifying GVHD cascade. RIPK3 deletion or genetically inactivating RIPK1 in recipient mice reduced GVHD. RIPK1/RIPK3 activates MLKL-dependent necroptosis to promote GI injury, however, MLKL deficiency merely delayed onset of GVHD without reducing its-related mortality. We discovered a functional role of RIPK1/RIPK3 in sustaining alloreactive T cell responses independently of MLKL, leading to GVHD cascade in the GI tract and the subsequent systemic inflammation. Pharmacological inhibition of RIPK1 reduces GVHD and restores intestinal homeostasis. Thus, RIPK1/RIPK3-mediated cell death-dependent and -independent action in IECs converts intestinal GVHD to a systemic disease, making it an excellent target for GVHD prevention and treatment.

Necroptosis: Molecular Mechanisms and Disease Implications

You-Sun KIM

Ajou University

Biography:

You-Sun Kim is a Professor at Department of Biochemistry, Ajou University School of Medicine, Korea. She received her PhD degree from Pusan National University in 2002. She received her postdoctoral training in the National Cancer Institute, National Institutes of Health, USA. She established her academic career at Ajou University School of Medicine, from Assistant Professor, Associate Professor to Full Professor. Her main research interests are in the field of cell biology, focusing on inflammation, anti-tumoural immunity, and cell death, especially necroptosis. Her group has made important contributions to the necroptosis research, from the molecular mechanisms to therapeutic target for inflammatory diseases and cancer. She has published more than 80 research papers, including *Nature Immunology*, *Molecular Cell*, *Cell Research*, and *Molecular Cancer* as a corresponding author. She was the Scientific Committee Member of the 15th International TNF meeting. Dr. Kim also contributes to the Korean Society for Biochemistry and Molecular Biology by serving as an Editor of BMB Reports.

Abstract:

Necroptosis is distinguished from apoptosis in that it does not require caspases, and unlike apoptosis, necroptosis directly results in plasma membrane rupture. Necroptotic cells may play multiple roles in innate immunity and shape subsequent adaptive immunity through the release of endogenous danger signals known as damage-associated molecular patterns (DAMPs), which interact with pattern recognition receptors (PRRs) of innate immune cells to prime immune cells to respond to pathogens and potentially harmful cells, such as those that are infected or tumourigenic. Receptor-interacting protein kinase-3 (RIP3, or RIPK3) is an essential protein for necroptosis, along with its upstream sister kinase RIPK1, which it interacts with via a homotypic interaction motif (RHIM). Mixed Lineage Kinase Domain-like protein (MLKL) is an essential target of RIPK3 kinase activity in necroptosis. The kinase activity of RIPK3 is required for downstream signaling events in necrotic cell death which is canonical function. Over the years, our understanding of a core necroptotic pathway consisting of RIPK3 activation increased substantially, but the recent discovery indicates that RIPK3 kinase may functions through non-canonical pathway, and also suggests tissue-specific roles of RIPK3. In this seminal, I will discuss about the functions of RIPK3 in various human diseases.

Immunogenic Cell Death: The Good, the Bad and the Ugly

Francis Kaming CHAN

Zhejiang University

Biography:

Francis Ka-Ming Chan is a native of Hong Kong. He received his PhD degree in Molecular and Cell Biology at the University of California, Berkeley, and was a Miriam & Benedict Wolf Postdoctoral Fellow of the Cancer Research Institute at the National Institutes of Health (USA). Professor Chan started his independent research group at the University of Massachusetts Medical School, where he rose through the ranks to become Full Professor. In 2018, he was recruited to the Department of Immunology at Duke University School of Medicine, where he served as Full Professor and Vice Chair of Research. In 2022, he moved to the Zhejiang University Medical Center and Liangzhu Laboratory as a Principal Investigator. Professor Chan's research centers around the role of cell death in immune signaling, inflammation, and host-pathogen interaction.

Abstract:

Immunogenic cell death (ICD) such as necroptosis, pyroptosis and ferroptosis promotes inflammation and is strongly associated with many disease pathologies. In addition to cell death, recent work indicates that ICD signal adaptors can often facilitate inflammation independent of cell death. Several key signal adaptors of ICD pathways are currently being tested as therapeutic targets in inflammatory diseases. Interestingly, an increasing number of pathogens have been found to encode inhibitors that interfere with host cell ICD. In this seminar, we will discuss the molecular mechanisms of ICD and their biological functions. We will also discuss strategies employed by pathogens to interfere with host cell ICD.

Session NINE
G Protein-coupled Receptor: Structure, Signaling and Diseases

Session Chair: Leo LEE
Co-Chair: Yang DU

Structure, Function and Drug Discovery of G Protein-coupled Receptor in Nervous System

Yang DU

The Chinese University of Hong Kong, Shenzhen

Biography:

Prof. Yang Du obtained PhD degree from the University of Science and Technology of China, and then went to Stanford University for postdoctoral training. During this period, he was awarded a full post-doctoral fellowship from the American Heart Association. He also obtained the position of assistant professor in the School of Medicine at the University of Michigan, Ann Arbor. His main research centers on the structure, function and drug discovery of G protein-coupled receptor (GPCR). Professor Du has published more than 60 high-quality papers, including *Cell, Science, Nature, Nature Comm, Science Adv, Cell Research* and *JACS*. He is currently an assistant professor and assistant dean in the School of Medicine at the Chinese University of Hong Kong, Shenzhen, and a principal investigator at the Kobilka Institute for Innovative Drug Discovery. Professor Du has been enrolled into talent programs among different levels such as National Chang-Jiang scholar and Guangdong Zhu-Jiang scholar.

Abstract:

Neuropsychiatric disorders are multifactorial disorders with diverse aetiological factors. Identifying treatment targets is challenging because the diseases are resulting from heterogeneous biological, genetic and environmental factors. Nevertheless, the increasing understanding of G protein-coupled receptor (GPCR) opens a new possibility in drug discovery. Harnessing our knowledge of molecular mechanisms and structural information of GPCRs will be advantageous for developing effective drugs. I will briefly introduce some recent work in my lab for studying structure and function of several G protein-coupled receptors in nervous system and how it guide novel drug discovery for the treatment of neuropsychiatric disorders.

Exchange Proteins Activated by Cyclic AMP and Their Role in Diverse Function and Diseases

Sookja Kim CHUNG

Macau University of Science and Technology

Biography:

Professor of the Faculty of Medicine and Dr. Neher's Biophysics Laboratory for Innovative Drug Discovery at the Macau University of Science and Technology (M.U.S.T.). Professor Chung graduated from the University of Illinois College of Medicine with a doctoral degree, she worked at Northwestern University Medical Center and later worked at The Rockefeller University in New York. She then moved to The University of Hong Kong (HKU), where she was the coordinator and teacher for MBBS Histology and system block coordinator. She also served as the member of medical Faculty Higher Degree Committee for postgraduate program and trained number of postgraduate students and junior academic staff. As an active researcher, she carried out numerous research projects with the successful funding from HK government and industry partners. She also taught at the Beijing Normal University-Hong Kong Baptist University United International College (UIC) for a year, before joining M.U.S.T. in 2019. Currently, she is the coordinator and teacher for Yr. 1 and Yr. 2 program and overseas the pathology curriculum. She serves (or served) as an Honorary Professor at Air Force Military Medical University in Xi'an, PRC; Shanghai Jia Tong University, PRC; Korea University College of Medicine, Korea; Adjunct Professor at UIC an Honorary Professor at Chung-Nam Medical University in South Korea and School of Biomedical Sciences, HKU, where she is currently a member of the State Key Laboratory of Pharmaceutical Biotechnology, HKU.

Abstract:

Currently, obesity and diabetes mellitus with their secondary complications contribute to the biggest and serious epidemic, which contribute to premature morbidity and mortality. Clearly, there is a therapeutic need for controlling the blood glucose level to alleviate complications and to provide a better quality of life for these patients. Hyperglycemia is due to insulin resistance, defective insulin sensitivity, and loss of insulin producing cells. Earlier, we reported that the analogue of the intestinal hormone glucagon-like peptide (GLP-1), Exendin-4, at high dosage can increase early insulin secretion in beta cells from embryonic stem cells by increasing the expression of insulin 1, Pdx-1 and exchange proteins directly activated by cAMP 1 and 2 (Epac1 and Epac2, respectively). The Epac1 and Epac2 are specific guanine nucleotide exchange factors for the Ras GTPase, Rap1 and Rap2, and downregulation of Epac function diminishes stimulatory effects of GLP-1 on beta cell Ca2+ signaling and insulin secretion, suggesting coupling of Epac to insulin secretion via GLP-1 receptor, which is a class B G protein-coupled receptor (GPCR) that mediates the action of peptide hormone, GLP-1. Previously, we have generated embryonic stem cells and mice with wild type, heterozygous and homozygous deletion of Epac1 gene. Epac1 deficient embryonic stem cells showed less number of glucose-responding beta cells and insulin secretion. The Epac1 knockout mice has the metabolic syndrome and are more likely to develop diabetes mellitus. On the other hand, we reported that Epac2 gene in mice and human is involved in anxiety and depression. With the Omic studies using these Epac genes engineered cells and mice, we were able to identify the role of Epac in diverse cellular processes and systemic function and dysfunction, which will be discussed in the meeting.

Multi-omics in MicroRNA-related Biomarker and Drug Target Discovery

Hsien-Da HUANG

The Chinese University of Hong Kong, Shenzhen

Biography:

Prof. Hsien-Da Huang is a presidential chair professor and associate dean of student affairs at the School of Medicine, and the executive director of Warshel Institute for Computational Biology, The Chinese University of Hong Kong, Shenzhen. He received PhD at Department of Computer Science and Information Engineering, National Central University, Taiwan, in 2003. Prof. Huang's research group majorly focuses on biological multi-disciplinary research topics, including Bioinformatics, Genomics, Metagenomics & Microbiome, Intelligent Biomedical Technologies (Drug Development, Genetic Test, & Precision Medicine), AI & Machine Learning, and Biological Database Design & Development. He published more than 170 peer-reviewed publications, mostly in prestigious journals, including *Science*, *Molecular Cell*, *Circulation*, *The Journal of Clinical Investigation*, *PLoS Biology*, *Hepatology*, *Cancer Research*, and *Nucleic Acids Research*.

Abstract:

High-throughput Sequencing, Mass Spectrometry (MS), and Data-driven Bioinformatics platforms, notably genomics, transcriptomics, proteomics, and metabolomics, facilitate the integrative analysis for biomarker and drug target discovery. With an emphasis on microRNA-mediated regulations involving diseases, we have developed several databases and computational platforms for identifying crucial disease-related genes with diagnostic values and drug development potentials. Besides, pathways regulating microRNAs' expressions have high prospects to be deeply investigated for therapeutics development.

Development of Oral Polypeptide Drug Targeting GPRC6A for Nonalcoholic Steatohepatitis

Pei-Gen REN

Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences

Biography:

Dr. Ren has worked in SIAT, CAS for 12 years. Before that, Dr. Ren finishhed his training in Institute of Microbiology, CAS, RIKEN, and Stanford University as a biologist. The research interesting of Ren Lab now is focusing on mebabolism related-G protein coupled receptors (GPCRs) and their biofunctions and mechanisms. Dr. Ren and his lab has been working on the signaling transduction between peptide ligands and their GPCRs for 20 years.

Abstract:

TBC

Preferential Binding of G Protein to the MT1 Protomer of the MT1/MT2 Heterodimeric Melatonin Receptor Complex

Yung Hou WONG

The Hong Kong University of Science and Technology

Biography:

Prof. Wong is Dean of Science and Chair Professor of Life Science at the Hong Kong University of Science and Technology (HKUST). He also serves as the Director of the Molecular Neuroscience Center at HKUST. Prof. Wong obtained his PhD in Pharmacology from the University of Cambridge and conducted postdoctoral training at the University of California San Francisco. His research is focused on the delineation of the mechanisms of cell signaling, particularly those involving the G protein-coupled receptors (GPCRs). He has made significant contributions in elucidating the molecular pharmacology of many GPCRs of therapeutic value, including those for opioid peptides, melatonin, and chemokines. Prof. Wong's group has demonstrated that many GPCRs can regulate gene transcription, cell proliferation and differentiation via complex signaling networks, and integrated these functional characteristics into high-throughput drug screening platforms. Prof. Wong also serves as an Editor-in-Chief of *FASEB BioAdvances*.

Abstract:

Melatonin is a neuroendocrine hormone that regulates the circadian rhythm and numerous physiological activities through activation of G protein-coupled receptors (GPCRs). The two GPCRs subtypes for melatonin (MT1 and MT2) have been demonstrated to form functional dimers between themselves or with other GPCRs, and emerging evidence point to a preferential formation of the MT1/MT2 heterodimer. Since the signalling capacity of the two melatonin receptor subtypes are not identical, it is pertinent to establish whether both protomers can signal simultaneously or if only one of them is functional. To gain insight on the preferred binding of G proteins to the heterodimer, various combinations of MT1, MT2, and Gi protein crystal structures were docked against each other by using RosettaDock and RosettaMPdock. Computational analyses of Gibbs free energy, dissociation constants, and molecular visualization of the heterodimer/G protein complexes collectively predict that the heterodimer is unlikely to bind two G proteins simultaneously, and that the G protein may preferentially associate with the MT1 protomer. Biased signalling via the MT1 protomer of the MT1/MT2 heterodimer was subsequently demonstrated in cell-based cAMP and Ca2+ mobilization assays. The use of signalling defective R3.50 mutants also revealed that the MT1 protomer may serve as the predominant functional unit of the MT1/MT2 heterodimer. These results support the notion that stable heterodimeric receptor/G protein complexes can be formed prior to agonist binding, and only one G protein may be preferentially bound to one of the protomers in the melatonin receptor heterodimer. In tissues and cells where both MT1 and MT2 receptors are co-expressed, the formation of MT1/MT2 heterodimers may limit MT2 signalling and alter the pharmacological action of melatonin (Supported by grants AoE/M-604/16, T13-605/18-W and ITCPD/17-9)

Session TEN
Molecular Mechanism and Precise Diagnosis and Treatment of Cancer

Session Chair: Kai MIAO

Nanoproteomics-based Biomarker Discovery and Cancer Diagnostics

Yuan LIU

Institute of Basic Medicine and Cancer, Chinese Academy of Sciences

Biography:

Yuan Liu, a principal investigator from the Hangzhou Institute of Medicine, Chinese Academy of Sciences. He obtained his PhD from Department of Chemistry at the University of Florida in December 2016. He received his postdoc training in Professor Xiaoyuan Chen's lab at the National Institute of Health and Professor Omid Farokhzad's lab at Harvard Medical School. In May 2021, he joined the Hangzhou Institute of Medicine. His research focuses on nanoproteomics, biomarker discovery, aptamer, and intelligent molecular cancer diagnosis.

Abstract:

TBC

Targeting UPS for Cancer Therapy: New Mechanisms and New Strategies

Jiangjiang QIN

Institute of Basic Medicine and Cancer, Chinese Academy of Sciences

Biography:

Dr. Jiang-Jiang Qin is currently a Professor of Cancer Pharmacology at Hangzhou Institute of Medicine (HIM), Chinese Academy of Sciences. He serves as the Deputy Director of Zhejiang Key Lab of Prevention, Diagnosis, and Therapy of Upper Gastrointestinal Cancer. He is also the Deputy Director of Key Laboratory for Molecular Medicine and Chinese Medicine Preparations. Dr. Qin received his B.S. degree in Pharmacy (2006) and PhD in Biomedical Engineering with the highest honor (2011) from Shanghai Jiao Tong University. His laboratory focuses to discover new cancer biomarkers and drug targets by applying innovative bioinformatics approaches, elucidate the molecular mechanisms underlying the development, progression, metastasis, and drug resistance of human cancer, especially gastric and pancreatic cancer, and develop novel, effective, and safe anticancer agents by utilizing state-of-the-art technologies. Dr. Qin has published more than 120 research papers and reviews; some of them have been published in high-impact journals, including *Nature Medicine, Nature Communications, Gastroenterology, Molecular Cancer, Cancer Research, Clinical Cancer Research* etc. His research has been funded by the National Key R&D Program of China, NSFC, Zhejiang Provincial NSF, etc.

Abstract:

The ubiquitin proteasome system (UPS) is vital for protein degradation and signal transduction. Its dysregulation has been linked to cancer and other diseases. It has been often observed that UPS members, including ubiquitin-activating enzymes (E1), ubiquitin-conjugating enzymes (E2), ubiquitin ligases (E3), and deubiquitinases (DUB) are frequently mutated and/or overexpressed in human cancer, contributing to cancer proliferation, migration, immunosuppression, and drug resistance. Our laboratories have a long-term interest in demonstrating the roles of UPS members, especially E2 (UbcH5c, etc.) and E3 (MDM2, FBXO44, etc.) in human cancer and developing novel small-molecule inhibitors and degraders for treating human cancer, especially pancreatic and gastric cancer. We have designed and developed a novel MDM2 inhibitor, termed SP141, that can directly bind to the RING domain of MDM2 and induce its ubiquitination and proteasomal degradation. We have also identified a dual MDM2 and NFAT1 inhibitor, named MA242, which can inhibit NFAT1-mediated MDM2 transcription and induce MDM2 protein degradation, thereby inhibiting MDM2 at both mRNA and protein levels. In our recent studies, we identified a novel UbcH5c inhibitor DHPO, which directly binds to this E2 enzyme and inhibits its downstream signaling pathways. All these compounds have been shown excellent anticancer efficacy *in vitro* and *in vivo*. Moreover, our labs have been developing new targeted protein degradation strategies and small-molecule degraders, which have shown excellent degradation efficacy for target proteins, although their anticancer activity and safety should be further evaluated. Based on these studies, we have established successful collaborations with basic and clinical scientists, physicians, clinicians, and industries. Our long-term goals are to translate basic science discoveries into innovative diagnostic and therapeutic strategies, finally improving the care and management of patients with malignant tumours, especially gastric and pancreatic cancer.

Tumour Targeting Aptamer Drug Conjugate and Nano Drug Delivery System

Xiangsheng LIU

Institute of Basic Medicine and Cancer, Chinese Academy of Sciences

Biography:

Dr. Xiangsheng Liu is a Professor at Zhejiang Cancer Hospital, Hangzhou Institute of Medicine (HIM), Chinese Academy of Sciences, China. He received his PhD in polymer chemistry and physics from Zhejiang University in 2014, and then gained Postdoctoral training and further worked as a project scientist at UCLA until he joined HIM in Oct, 2020. His current research interests focus on aptamer drug conjugate (ApDC), nucleic acid delivery, and nanomedicine for cancer and other serious diseases. Dr. Liu's research has been published in many international Journals, including Journal of Clinical Investigation (JCI), ACS Nano, Advanced Science, Nature Communications, Nano Letters etc. He has published > 70 peer-reviewed papers, with >5000 citations (Google Scholar). His patented SILICASOME irinotecan nano drug technology is undergoing clinical transformation in the United States for pancreatic and colon cancer.

Abstract:

This presentation will mainly share the team's research work on tumour targeting aptamer drug conjugate (ApDC) and anti-tumour nanomedicine. Aptamers are a class of single-chain oligonucleotide molecules that can specifically recognize targets. They have similar recognition function to antibodies, but they can be efficiently prepared by chemical solid phase synthesis, so they are also called "chemical antibodies". Based on the targeted recognition function of nucleic acid aptamers, our team pioneered the concept of ApDC in the world. This report will share the latest progress of our team in the research of ApDC. Nanomedicine is another strategy for efficient targeted drug delivery, this report will also share our research on targeted delivery using a new class of nano drug carrier silicasome, i.e., lipids coated mesoporous silica nanoparticles, and their application for cancer treatment in a variety of gastrointestinal tract tumours.

Design Optogenetic Toolbox for Deep Understanding Intracellular Organelles Communications and Remote Control of Programmed Cell Death

Ji JING

Institute of Basic Medicine and Cancer, Chinese Academy of Sciences

Biography:

Dr. Ji Jing obtained his PhD in Biomedical Science and completed his Postdoctoral training from Texas A&M University. He started his own lab in Hangzhou Institute of Medicine (HIM), Chinese Academy of Sciences, in 2021. His research interests focus on design and implementation optogenetic tools to manipulate the function of intracellular organelles and their communications with the goal to develop new methods to study principles of cell signaling and behavior, ultimately achieving better treatment and prevention strategies for clinical research and applications.

Abstract:

Herein, a set of optogenetic tools that enable rapid and reversible control inter-membrane tethering at membrane contact sites (MCSs) and photoswitchable necroptosis and pyroptosis in live cells with varying kinetics, is introduced. MCSs are specialized subcellular compartments formed by closely apposed membranes from two organelles. These intermembrane contact sites constitute important intracellular signalling hotspots to mediate a plethora of cellular processes, including calcium homeostasis, lipid metabolism, membrane biogenesis and organelle remodeling. However, there are short of tools for reversibly manipulating the assembly of MCSs to study their communications. Optogenetics offers excellent opportunities for precise spatial and temporal control of physiological processes in live cells and tissues. We therefore take an optogenetic engineering approach to mediate a plethora of cellular processes, including calcium homeostasis, lipid metabolism, membrane biogenesis and organelle remodelling. In addition, we also developed light-induced non-apoptotic tools (LiPOPs) to control programmed cell death, ultimately achieving better treatment and prevention strategies for clinical research and applications.

Session ELEVEN
Spatial Omics Biology

Session Chairs: Edwin CHEUNG and Peng WANG

Large-field of View, High-Resolution Spatially Resolved Transcriptomics Using DNA Nanoball Patterned Array

Longqi LIU

BGI Genomics

Biography:

Dr. Longqi Liu is the chief scientists on sing-cell omics at BGI·Research. He obtained his PhD research at Chinese Academy of Sciences. There he studied the epigenetic mechanism underlying somatic cell reprogramming to pluripotency. He then moved to BGI·Research as a group leader, focusing on development of single-cell multi-omics technologies. He has won the first prize of the Natural Science of Guangdong Province, the first prize of the Chinese Postdoctoral Science Foundation, and the Dean's Excellence Award of the Chinese Academy of Sciences. Dr Liu leaded the development of DNBelab C4 high-throughput single cell microfluidic system, mapped the first cell atlas of non-human primate (*Nature*, 2022), developed spatial transcriptomic platform Stereo-seq and mapped the Spatiotemporal transcriptomic atlas of embryogenesis in mouse, fly and zebrafish (*Cell*, 2022, *Developmental Cell*, 2022[a], *Developmental Cell*, 2022[b]).

Abstract:

High-throughput profiling of in situ gene expression represents a major advance towards the systematic understanding of tissue complexity. Applied with enough capture area and high sample throughput it will help to define the spatio-temporal dynamics of gene expression in tissues and organisms. Yet, current technologies have considerable bottlenecks that limit widespread application. We have combined DNA nanoball (DNB) patterned array chips and in situ RNA capture to develop Stereo-seq (SpaTial Enhanced REsolution Omics-sequencing). This approach allows high sample throughput transcriptomic profiling of histological sections at unprecedented (nanoscale) resolution with areas expandable to centimeter scale, high sensitivity and homogenous capture rate. As proof of principle, we have applied Stereo-seq to study the kinetics and directionality of transcriptional variation in embryogenesis. We used this information to gain insight into the molecular basis of regional specification and cell fate diversification. Our panoramic atlas constitutes an essential resource to investigate longstanding questions concerning normal and abnormal development.

Single Cell Proteomic Analysis Techniques and Clinical Applications

Xianting DING

Shanghai Jiao Tong University

Biography:

Dr. Xianting Ding is professor at School of Biomedical Engineering, deputy director of Institute for Personalized Medicine, Shanghai Jiao Tong University. He is elected into the Chinese Top Elite Researcher Program, China Special Researcher Support Program, Qiushi Foundation Elite Investigator. He received his PhD degree from Department of Mechanical Engineering at University of California, Los Angeles (UCLA). His research interests focus on developing Personalized Therapy and Precision Medicine, including: 1) developing bio-sensors for early detection of cancer, infectious disease, and metabolic diseases; 2) developing personalized treatment with optimized drug combinations. He participated in the early investigation and development of 3 multi-million-USD international research centers, including Institute for Cell Mimetic Space Exploration (CMISE, funded by NASA), Center for Cell Control (CCC, funded by NIH) and Institute for Personalized Medicine (IPM, funded by Chinese Central Organization Department). He is on the editorial board for 6 international journals, has published over 120 peer reviewed journal papers and has filed 70 national or international patents.

Abstract:

The human body is a very complex system, so the occurrence and development of diseases are often accompanied by multiple target abnormalities of genes, transcription, protein, metabolism, immune cell population and many other omics. How to make full use of the patient's limited blood or tissue samples, systematically monitoring the simultaneous changes of multiple ensembles of multiple targets on each cell is a daunting task. Our team has been working on the joint detection of multiple targets for complex diseases and the optimal compatibility of multi-target combination drugs. The single cell mass spectrometry (CyTOF), single cell westernblot (SCWB), and microfluidic electrochemical technology that the laboratory has been engaged in have gradually realized the joint detection of multiple omics information on a single cell scale. At the same time, the feedback system control technology (FSC), Phenotypic Personalized Medicine (PPM) and Parabolic Response Surface (PRS) developed by the laboratory have been gradually realized. From dozens of or even hundreds of candidate drug molecules, the combination of the most synergistic drugs is rapidly optimized at the cost of a very small number of experiments. This presentation will introduce the current technology development and clinical applications for single cell multiplex diagnosis for personalized medicine.

Statistical Methods for Spatial Transcriptomics

Xiang ZHOU

University of Michigan

Biography:

Dr. Xiang Zhou is an Associate Professor in the Department of Biostatistics in the School of Public at the University of Michigan. He is also an Assistant Director at the University of Michigan Precision Health. He has been an Associate Professor since 09/2019. Dr. Zhou joined the department as an Assistant Professor in 2014 and became the John G. Searle Assistant Professor in the department in 2018-2019. Before joining UM, he was a Williams H. Kruskal Instructor in the Department of Statistics at the University of Chicago in 2013-2014. He received an MSc degree in statistics in 2009 (adviser: Prof. Scott Schmidler) and a PhD degree in neurobiology in 2010 (adviser: Prof. Fan Wang), both from Duke University. He was a postdoctoral scholar working with Prof. Matthew Stephens at the University of Chicago during 2010-2013.

Abstract:

Spatial transcriptomics is a collection of groundbreaking new genomics technologies that enable the measurements of gene expression with spatial localization information on tissues or cell cultures. Here, I will discuss a few new statistical methods that our group has recently developed for analyzing spatial transcriptomics data. Specifically, I will first talk about SPARK, a method that allows for rigorous statistical analysis of spatial expression patterns in spatial transcriptomics. I will talk about a non-parametric extension of SPARK, called SPARK-X, for rapid and effective detection of spatially expressed genes in large spatial transcriptomic studies. If time allows, I will also talk about a spatially informed cell type deconvolution method, CARD, that leverages cell type specific expression information from single cell RNA sequencing for the deconvolution of spatial transcriptomics.

Session TWELVE
Natural Product-based Drug Discovery

Session Chairs: Xiuping CHEN and Ying WANG

Roles of University Technology Transfer in Biomedical Business

Hong PENG

Yale University

Biography:

Hong Peng, PhD, MBA, is a Director of Business Development at Yale Ventures. She has over 25 years of experience in intellectual property management and business development. She has a robust life science background, and extensive expertise in negotiating intellectual property-related contracts such as patent licenses, options, dispute settlement, sponsored research agreements, and corporate alliances. Hong joined Yale University in 2006 and has been managing a large portfolio of intellectual property in life sciences. She has been instrumental in establishing various pharmaceutical alliances and forming new ventures based on technologies generated at Yale University.Prior to her current position, Hong was Director of Patents and Licensing at Lindsley F. Kimball Research Institute of New York Blood Center, where she led an operation with an annual royalty income of $60 million. She has also worked as a Licensing Associate at the Memorial Sloan-Kettering Cancer Center. Hong holds a PhD in Molecular Biology from Cornell University, an MBA from Columbia University, and a BSc in Biology from Peking University in China.

Abstract:

Dr. Hong Peng is a director of business development of Yale Ventures, a tech transfer operation of Yale University. With some real-world examples, this presentation will cover some basics of intellectual property management and commercialization at academic institutions in the United States.

The Study on Anti-Glioblastoma Effect and Its Mechanism of Sinomenine Ester Derivative

Jinhua WANG

Peking Union Medical College

Biography:

Jinhua Wang, PhD, Professor, vice director of National Center for Pharmaceutical Screening.In 2004, he received his PhD from Peking University. From 2004 to 2006, he worked as a postdoctoral researcher at the Institute of Materia Medica, Chinese Academy of Medical Sciences. From 2006 to 2015, he worked as research associate, medical scientist, assistant professor in Case Western Reserve University and John Wayne Cancer Institute in the United States. In 2015, he returned to China and was appointed as the "Xiehe Scholar" distinguished Professor of Peking Union Medical College, and the Chief Scientist of the Collaborative Innovation Team of the Medical and Health Science and Technology Innovation Project of the Chinese Academy of Medical Sciences. He chaired a few of research funds, such as the National Natural Science Foundation of China, the Natural Science Foundation of Beijing and the "13th Five-Year Plan" major new drug creation of the Ministry of Science and Technology et al. Up to now, he published more than 100 peer-reviewed papers, including *Journal of Clinical Investigation (JCI), Signal Transduct Target Ther, Journal of the National Cancer Institute (JNCI), Journal of Clinical Oncology (JCO), PNAS, Cancer research, Oncogene, Acta Pharmaceutica Sinica B, Cancer letter* et al.

Abstract:

Glioblastoma multiforme (GBM) in the central nervous system is the most lethal advanced glioma and currently there is no effective treatment for it. Studies of sinomenine, an alkaloid from the Chinese medicinal plant, Sinomenium acutum, showed that it had inhibitory effects on several kinds of cancer. Here, we synthesized a sinomenine derivative, sino-wcj-33 (SW33), tested it for antitumour activity on GBM and explored the underlying mechanism. SW33 significantly inhibited proliferation and colony formation of GBM and reduced migration and invasion of U87 and U251 cells. It also arrested the cell cycle at G2/M phase and induced mitochondria-dependent apoptosis. Differential gene enrichment analysis and pathway validation showed that SW33 exerted anti-GBM effects by regulating PI3K/AKT and AMPK signaling pathways and significantly suppressed tumourigenicity with no obvious adverse effects on the body. SW33 also induced autophagy through the PI3K/AKT/mTOR and AMPK/mTOR pathways. Thus, SW33 appears to be a promising drug for treating GBM effectively and safely.

Immune Checkpoint HLA-E:CD94-NKG2A Mediates Evasion of Circulating Tumour Cells from NK Cell Surveillance

Hubing SHI

Sichuan University

Biography:

Dr. Hubing Shi graduated from Tsinghua University, where he got his PhD diploma. He continued his postdoctoral research by joining a translation medical group leading by Dr. Roger Lo and Antoni Ribas in 2009 at UCLA. His postdoc research focused on how tumours escape from oncogene-targeted therapy and immune checkpoint blockade. He reported several BRAFi resistant mechanisms (*Nature*. 2010, *Nature Commun*. 2012, *Nature*. 2012, *Cancer Discovery* 2014 a/b; *Cancer Cell*, 2015; *Cell*, 2015). The combinatorial regimens proposed in these literatures not only inspire clinical trials but also change the NCCN guidelines of melanoma therapy. He developed his independent research career at West China Hospital, Sichuan University. His current research interests include: 1) identification of novel tumour-immune interaction (Cancer Cell, 2023), 2) tumour precision medicine (*STTT*, 2022; *Cell Reports Medicine*, 2022), 3) combination between ICB and targeted therapy (*Advanced Functional Materials*, 2019; *Nano Today*, 2022; *J. Control. Release*, 2020, 2022), etc.

Abstract:

Circulating tumour cells (CTCs), shed by primary malignancies, function as “seeds” for distant metastasis. However, it is still largely unknown how CTCs escape immune surveillance. Here, we characterize the transcriptomes of human pancreatic ductal adenocarcinoma CTCs, primary, and metastatic lesions at single-cell scale. Cell-interaction analysis and functional studies *in vitro* and *in vivo* reveal that CTCs and natural killer (NK) cells interact via the immune checkpoint molecule pair HLA-E:CD94-NKG2A. Disruption of this interaction by blockade of NKG2A or knockdown of HLA-E expression enhances NK-mediated tumour cell killing *in vitro* and prevents tumourmetastasis *in vivo*. Mechanistic studies indicate that platelet-derived RGS18 promotes the expression of HLA-E through AKT-GSK3b-CREB signaling, and overexpression of RGS18 facilitates pancreatic tumour hepatic metastasis. In conclusion, platelet-derived RGS18 protects CTCs from NKmediated immune surveillance by engaging the immune checkpoint HLA-E:CD94-NKG2A. Interruption of the suppressive signaling prevents tumour metastasis *in vivo* by immune elimination of CTCs.

Progress in the Personalization of Tumour Chemotherapeutic Drug

Liwu FU

Sun Yat-Sen University

Biography:

Professor Liwu Fu is MD, PhD, from Cancer Center, Sun Yat-sen University. He is mainly engaged in the research fields of cancer pharmacology including tumour stem cells and their drug resistance, and the mediation and reversal of multi-drug resistance in tumours.and the individualized chemotherapeutic drugs. He got 863, 973 projects, major research and development projects, national Natural Science Foundation of China etc. supports and published mor than 280 papers. He won the Chinese Pharmacological Society-Servier Award (1997), the first prize of Scientific and technological Achievements of China Anti-Cancer Association (2013, ranked first), the first prize of Guangdong Science and Technology Progress Award (Natural Science) (2012, ranked first). He is an Elservier released "China highly cited Scholars" in 2020-2023.

Abstract:

As we know different types of tumours have different sensitivity to anti-cancer drugs; even if the clinical stage, pathological type and basic status of patients are the same, different individual patients have different sensitivity to chemotherapeutic drug, which required that the chemotherapy drugs (regimen) must be individualized. But many patients still received the invalid treatment. There are two main ways to realize the personalization of chemotherapeutic drugs, one is the guidance of genetic information and the other is drug sensitive test. This paper mainly introduces the establishment and application of the drug sensitivity test system with primary tumour microtissue block culture, which has the advantages of simple, fast (5 days), high success rate（> 90%) and reliable results.

Therapeutic Targets of Metabolic Disorders - What's New?

Hoi Leong Xavier WONG

Hong Kong Baptist University

Biography:

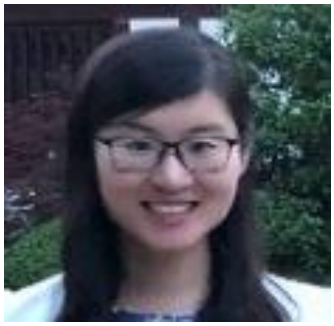
Dr. Xavier Wong obtained his Bsc degree in Biochemistry from the University of Hong Kong in 2009. He completed his PhD degree at the Department of Biochemistry, the University of Hong Kong in 2013. Currently, he is a tenured Associate Professor at the School of Chinese Medicine, Hong Kong Baptist University. His research focuses on the characterization of the proteolytic enzymes that control extracellular matrix remodeling during growth and development. As the regulation of proteinase expression underlies various important biological processes, elucidating these fundamental processes is crucial for our understanding of cell behavior within the confines of the extracellular matrix encountered in both physiological and pathological conditions. Another area of research interest has focused on the role of host-microbe interaction. The human meta-organism has evolved as a unity of both eukaryotic and prokaryotic cells. Dr. Wong's research team is exploring the mechanisms by which this co-evolution has led to homeostatic host-microbial mutualism.

Abstract:

Obesity and diabetes are major causes of morbidity and mortality. Obesity is known to be the main risk factor for various non-communicable diseases, in particular type 2 diabetes. There is an ongoing need to identify non-invasive therapeutic approaches for the management of obese patients with type 2 diabetes to achieve their glycemic and weight loss goals. Recently, mutations in MT1-MMP (MMP14), a membrane bound metalloproteinase responsible for extracellular matrix remodeling and pericellular proteolysis, have been associated with human obese and diabetic traits. In this talk, the role of MT1-MMP in energy and glucose homeostasis and the molecular mechanism by which MT1-MMP regulates body weight and insulin sensitivity will be discussed.

Session THIRTEEN
Targeting Gut Microbiota and Metabolism for Cancer Immunomodulation

Session Chair: Elaine LEUNG



Gut Microbiota, Metabolites and Fatty Liver Diseases

Xiang ZHANG

The Chinese University of Hong Kong

Biography:

Dr. Zhang's research interests are mainly non-alcoholic fatty liver diseases (NAFLD), especially for pathogenic mechanism, diagnosis, and treatment of non-alcoholic steatohepatitis and its related hepatocellular carcinoma. She has published over 50 papers (12 papers with impact factor > 30; H-index 27) in international peer-reviewed journals, including *Gastroenterology, Gut, J Hepatol, Cell Research*, and 3 book chapters. Her contributions to the advancement of NAFLD have been internationally recognized and she has obtained 20 awards including National Natural Sciences Award 2020; An Expertscape Expert in Fatty Liver 2022; and National Scholar Award in United European Gastroenterology Week 2015. Dr Zhang has delivered more than 20 presentations at major international conferences including DDW. She has obtained 7 competitive grants as the principal investigator in recent 2 years, including HMRF, NSFC and GRF. In 2022, she won NSFC Excellent Young Scientists Fund Non-Alcoholic Fatty Liver Disease which supports young scientists who have made significant contributions to fundamental research.

Abstract:

Non-Alcoholic Fatty Liver Disease (NAFLD) is the most common chronic liver disease worldwide. 12-40% of NAFLD patients could progress to its more severe subtype-non-alcoholic steatohepatitis (NASH), which can further develop to cirrhosis and hepatocellular carcinoma (HCC). NASH is a complex and progressive disease. Emerging evidence suggested that gut microbiota contributes to NASH and its associated HCC development through gut-liver axis. This talk will introduce our recent findings on complex link among diet, gene, microbiota, metabolites and the progression of NASH and NASH-HCC. In addition, our recent findings on the preventive and therapeutic role of drug in NASH as well as the role of probiotics in preventing NASH-HCC will be discussed.

Humanized Germ-free Animal Models and Their Roles in the Study of Microbiome Related Tumour Genesis and Development and Immunotherapy

Yuting YANG on behalf of Hong WEI

Sun Yat-Sen University

Biography:

Professor Wei is the chairman of the professional committee on germ-free animals of the Chinese Association for Laboratory Animal Sciences (CALAS) and pioneer in establishing large-scale germ-free animal technology system in China. His research focuses on germ-free animals and functional microbiome. By utilizing genetic engineering technology and germ-free animals to elucidate functions of host genome and microbiome and their interactions, he has built an innovative research system for the construction and application of animal models. He has undertaken the 973, 863, National Natural Science Foundation of China (NSFC) and other projects in the field of germ-free animals and genetically engineered pig models. He has published 140 peer-reviewed articles in journals including *Science* with a cumulative impact factor of 1014.847. As the editor-in-chief, he led the publication of Laboratory Animal Science as one of the first batch of national postgraduate teaching books recommended by the Ministry of Education, and the publication of *Medical Animal Experimental Technology* funded by the National Funds for Academic Publications in *Science and Technology* (NFAPST).

Abstract:

A growing body of evidence has demonstrated that the commensal microbiome is deeply involved in tumour genesis and development and as well as the host immune response. Therefore, precise screening and evaluating of functional bacterial strains as novel targets for cancer immunotherapy have attracted great enthusiasm from both academia and industry, which calls for the construction and application of advanced animal models to support translational research in this field. Integrating rederivation and humanization to generate humanized germ-free (GF) animals as preclinical models would make it possible to clarify the role of specific bacterial strains in immunotherapy and obtain preclinical findings that are more predictive for humans, leading to novel microbiome-based strategies for cancer immunotherapy.

Intestinal Microbiome and Disease Health

Di LIU

Wuhan Institute of Virology, Chinese Academy of Sciences

Biography:

Dr. Di Liu received his Doctoral degree in bioinformatics from Peking University. Currently, he is a professor and principal investigator at Wuhan Institute of Virology, Chinese Academy of Sciences. His research area includes virus genomics & evolution, and bioinformatics. In 2018, his group began the study of DNA data storage and was supported by the National Key R&D Program. Dr. Liu has published over 140 research articles in journals including *Nature, Lancet, New England Journal of Medicine, Cell Metabolisms*, etc. He achieved an H-index of 43 in 2022.

Abstract:

The gut microbiome has been shown to play an important role in human health and disease. Professor Liu has made a series of progress in studying the intestinal microbiome. He found that ginseng polysaccharides can regulate the gut microbiome and enhance the efficacy of immunotherapy for lung cancer. He also found that Klebsiella pneumoniae from the gut microbiome can produce endogenous ethanol, leading to increased blood ethanol concentration in the patient. All these studies provided evidence for exploring the link between the gut microbiome and health and disease.

Precision Medicine and the Mechanistic Basis of Combination Treatments for Liver Cancer

Carmen Chak-Lui WONG

The University of Hong Kong

Biography:

Dr. Carmen Wong is currently an Associate Professor and Principal Investigator in the Department of Pathology and State Key Laboratory of Liver Research at the University of Hong Kong. She is the program leader of the liver cancer program at Center of Oncology and Immunology at InnoHealth, Hong Kong. She obtained her PhD degree in the University of Hong Kong and completed her post-doctoral training in the Johns Hopkins University, studying the roles and molecular mechanisms of hypoxia (oxygen deprivation) in cancer metastasis. Her research team currently focuses on the immune microenvironment in liver cancer. Over the years, her work was published in *PNAS*, *Gastroenterology*, *Journal of Hepatology*, *GUT*, *Hepatology*, *Nature Communications*, *Cell Reports*, and the *Journal of Clinical Investigation*. She is the recipient of the Croucher Innovation Award, Outstanding Young Researcher Award of HKU, National Natural Science Foundation of China Excellent Young Scientist Fund, Hong Kong Young Scientist Award, the Best PhD thesis Awards of HKU, Croucher Fellowship, University of British Columbia (Canada) Alumni Builder Award. She is an elected member of the Hong Kong Young Academy of Science. She is the co-editor-in-chief of Hepatology Communications (AASLD).

Abstract:

TBC

Session FOURTEEN
Molecular Probes and Biosensors

Session Chairs: Xuanjun ZHANG and Xiaoqiang CHEN

Development of Fluorescent Polarization-based High Throughput Screening Assays

Zhizeng GAO
Sun Yat-Sen University

Biography:
Zhizeng Gao graduated from Shandong University with a bachelor's degree. From 2008 to 2013, he pursued a doctoral degree at the University of Alberta in Canada, and from 2013 to 2018, he conducted postdoctoral research at the University of British Columbia. Currently, he serves as an Associate Professor at the School of Marine Sciences, Sun Yat-sen University, where his primary research focus lies in the development and utilization of marine biological resources. Specifically, his research agenda centers on the dual objectives: (1) development of high throughput strategies for the utilization of marine biological resources, (2) elucidating the biosynthetic mechanisms of marine active natural products. Zhizeng's research contributions have been featured in various high-impact journals, including *Nature Chem Bio, JACS, Angew Chem, and JBC*, among others.

Abstract:
Fluorescent polarization-based assays are important tools for drug discovery and molecular biology research. These assays rely on the measurement of changes in fluorescence polarization of a labeled ligand as it interacts with its target molecule. The use of fluorescent polarization allows for a simple, sensitive and robust assay format, making it a popular choice for large-scale screening. In this talk, I will discuss our recent applications of fluorescent polarization-based assays for screening SARS-CoV-2 fusion inhibitors and glycosyltransferase inhibitors.

Recent Advances in ICG Near-Infrared Fluorescence Molecular Imaging in the Second Biowindow

Zonghai SHENG

Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences

Biography:

Professor Zonghai Sheng received his PhD (2010) degrees from Huazhong Agricultural University, China. Then, he worked as a postdoctoral fellow researcher from 2011 to 2013 at the Chinese Academy of Sciences (Supervisor: Prof. Lintao Cai). Since 2018, he has been a full professor at the Institute of Biomedical and Health Engineering (Prof. Hairong Zheng's group), Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences. His main research activities focus on nanoprobes and molecular imaging.

Abstract:

Indocyanine green (ICG) is a small water-soluble tricarbocyanine dye that was first approved by the US FDA for human imaging studies in 1958. Currently, ICG is widely used in clinical applications such as monitoring cardiac output, evaluating liver function, imaging blood vessels, lymphatic vessels and lymph nodes, and imaging tumours. Recent studies have found that the tail emission of ICG exceeds 1000 nm, entering the near-infrared second window (NIR-II, 1000-1700 nm) for imaging. Based on this discovery, ICG-based near-infrared second window fluorescent molecular imaging has received widespread attention in the fields of basic research and clinical applications. This report introduces the research history of ICG and the latest research progress in the field of optical molecular imaging, focusing on the application of ICG molecular imaging probes in NIR-II imaging. The report mainly includes: new methods to improve the NIR-II luminescence brightness of ICG, new technologies to enhance the *in vivo* circulation stability and disease targeting of ICG, and the preclinical and clinical applications of ICG's NIR-II fluorescence molecular imaging, as well as the challenges faced by the current development in this field.

Functional Dyes for Imaging and Detection Applications

Xiaoqiang CHEN

Nanjing Tech University

Biography:

Xiaoqiang Chen received his PhD in Applied Chemistry from Dalian University of Technology (China) in 2007. He joined Prof. Juyoung Yoon's group at Ewha Womans University (Korea) as a postdoctoral fellow in 2008. In March 2010 he moved to Nanjing Tech University, where he is currently a professor in College of Chemical Engineering. His current research interests mainly focus on fluorescent or colorimetric sensors for imaging and detection applications in biology and hydromechanics fields. So far, he has published 130+ academic publications, including *Chem. Rev., Chem. Soc. Rev., Acc. Chem. Res., Nature Protocols, JACS, Angew Chem. Int. Ed*. etc. These publications have been cited for more than 13000 times. He has also been selected into the list of "Chinese highly cited scholars" from 2018 to 2022.

Abstract:

Fluorogenic and colorimetric methods in conjunction with suitable probes are preferable approaches for the measurement and imaging of analytes and parameters in biology and fluid dynamics because these methods are rapidly performed, nondestructive, and highly sensitive, affording real information on the localization and quantity of the targets of interest. Based on the traditional dyes, after modification in structures we obtained various fluorescent and colorimetric probes for detecting biological species and enzyme activity, and imaging temperature distribution on surface of volatile solvents with high resolution.

Spatiotemporal Visualization of Bystander Activity of Antibody Drug Conjugates for Enhancing Solid Tumour Penetration

Peng GUO

Institute of Basic Medicine and Cancer, Chinese Academy of Sciences

Biography:

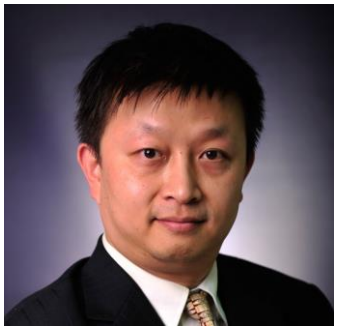
Dr. Guo graduated from Jilin University with a bachelor's degree in chemistry in 2005, received his PhD in analytical chemistry from the University of Florida in 2011, and conducted doctoral joint training at Stanford University from 2009 to 2011. From 2011 to 2020, he worked as a postdoctoral fellow and instructor at Harvard University and Boston Children's Hospital. In 2021, he joined Hangzhou Institute of Medicine, Chinese Academy of Sciences. His main research directions are drug target screening, antibody drug conjugates, extracellular vesicle-based therapeutics. So far, he has published more than 30 research papers and review articles, of which the representative work of the first author and corresponding author has been published in internationally renowned journals such as *PNAS, Nature Communications, Science Advances*, *Trends* in *Pharmacological Sciences*.

Abstract:

Antibody drug conjugate (ADC) has had a transformative effective on the treatment of many solid tumours, yet it remains unclear how ADCs exert bystander activity in the tumour microenvironment. Here, we directly visualized and spatiotemporally quantified the intratumour biodistribution and pharmacokinetics of different ADC components by developing dual-labeled fluorescent probes. Mechanistically, we found that tumour penetration of ADCs is distinctly affected by their ability to breach the binding site barrier (BSB) in perivascular regions of tumour vasculature, and bystander activity of ADC can only partially breach BSB. Furthermore, bystander activity of ADCs can work in synergy with co-administration of their parental antibodies, leading to fully bypassing BSBs and enhancing tumour penetration via a two-step process.

Session FIFTEEN
Neuroscience, Aging and Degenerative Diseases

Session Chair: Wenhua ZHENG
Co-Chair: Jiangang SHEN



Neurovascular Unit Roles in Neurodegeneration

Qing WANG

Southern Medical University

Biography:

Prof. Dennis Qing Wang is the Director of Department of Neurology, Zhujiang Hospital of Southern Medical University. He is also the member of SFN and APSN and he has won the “Leading Talent in Talents Project Guangdong High-level Personnel of Special Support Program” in 2016, and the “Outstanding Young Medical Talents of Guangdong” in 2018. He is the Associate Editor of Frontiers in *Aging Neuroscience* (IF:5.7), editor of Frontiers in *Cellular Neuroscience* (IF:6.06), and editorial Board Member of international journals (*Aging and Disease*). He has received more than 40 grant supports, including the 973 Project, National Key R&D Program of China, five National Natural Science Foundations of China. He has published more than 80 papers in international journals with H-index of 30, such as *EclinicalMedicine* (IF:17), Brain (IF:15.3), Progress in *Neurobiology* (IF:10.8)，*EBioMedicine* (IF:11.2), *Brief Bioinform* (IF:13.99), *Move Disord* (IF:10.8) and *Aging and Disease* (IF:9.96). Papers were cited more than 3900 citations.

Abstract:

Cystatin C (CYS C, Cst3) is an endogenous cysteine protease inhibitor that plays neuroprotective roles in neurodegenerative diseases. We aimed to explore the association of CYS C with Parkinson's disease (PD) models and investigate its involvement in the role of neurovascular units (NVUs) in PD neuro-pathogenesis. We used A53T α-synuclein (SNCA) transgenic mice and 6-hydroxydopamine-lesioned DAergic PC12 cells as experimental PD models to investigate the mechanisms behind this association. The injections of CYS C were administered to the right substantia nigra (SN) of A53T SNCA transgenic mice to measure the effects of CYS C in transgenic A53T SNCA mice. To explore the angiogenesis *in vivo* and *in vitro*, we used the chick embryo chorioallantoic membrane (CAM) assay and tube formation (TF) assay. We found that CYS C has a neuroprotective effect in this *in vivo* PD model. We observed increased VEGF, NURR1 and autophagy markers LC3B and decreased SNCA and apoptosis marker cleaved CASP3 in different brain regions of CYS C-treated A53T SNCA transgenic mice. *In vitro*, we observed that CYS C-induced VEGF, a secreted protein, attenuated 6-OHDA-lesioned DAergic PC12 cell degeneration by regulating p-PKC-α/p-ERK1/2-Nurr1 signaling and inducing autophagy. VEGF-mediated angiogenesis was markedly enhanced in the conditioned media of 6-OHDA-lesioned PC12 cells with CYS C-overexpression, whereas blockage of autophagy in CYS C-overexpressing PC12 cells significantly downregulated VEGF expression and the associated angiogenesis. Our data indicate that CYS C displays dual neuronal-vascular functions, promoting PC12 cell survival and angiogenesis via regulating the level of secreted VEGF in NVUs. Our study provides evidence that may aid in the development of an alternative approach for the treatment of PD through modulation of CYS C-mediated neuronal-vascular pathways.

Aging Rlated CSVD and Inflammation

Zhengqi LU

Sun Yat-Sen University

Biography:

Dr. Lu Zhengqi is the Director of the Department of Neurology and a doctoral supervisor at the Third Affiliated Hospital of Sun Yat-sen University. He is dedicated to clinical diagnosis and treatment of neurological disorders and scientific research. His main research focus is on neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease. He has made many important contributions in these fields. Dr. Lu's achievements in the research of neurodegenerative diseases have been widely recognized and praised. His research results have been published in many internationally renowned scientific journals, and he has received many national and provincial scientific and technological awards. As an outstanding clinician and scientist, Dr. Lu is committed to promoting the development of neuroscience and making more contributions to the prevention and treatment of neurodegenerative diseases.

Abstract:

Research Progress in Prehospital Neuroprotection of Acute Stroke

Xintong LIU

Guangdong No. 2 General Hospital

Biography:

Xintong-Liu Pd.D Chief Physician of Neurology

Director of the Department of Neurology and the Center for Cerebrovascular Disease of the Second People's Hospital of Guangdong Province, Tutor for postgraduates of Southern Medical University, Member of the Cerebrovascular Intervention Collaborative Group of the Neurology Branch of the Chinese Medical Association, Member of the Cerebral Blood Flow and Metabolism Branch of the Chinese Stroke Society, Member of the Neurointerventional Committee of the Neurology Branch of the Chinese Medical Doctor Association, Standing Member of the Neurology Branch of the Guangdong Medical Doctor Association, Standing Member of the Neurointerventional Committee of the Guangdong Medical Doctor Association, Member of the Standing Committee of the Cerebrovascular Disease Professional Committee of Guangdong Medical Association, Member of the Vertigo Group of the Neurology Branch of Guangdong Medical Association, Member of the Standing Committee of the Neurorepair and Intractable Diseases Committee of the Guangdong Stroke Society, Vice chairman of the Neurology Committee of the Guangdong Association of Integrative Traditional Chinese and Western Medicine, Chairman of the Interventional Neurology Branch of the Guangdong Clinical Medical Association, published more than 60 core journals and SCI papers

Abstract:

1. Domestic status quo of stroke
2. Pathophysiological mechanism of prehospital neuroprotection
3. Methods and measures of prehospital neuroprotection

Adiponectin Deficiency Accelerates Brain Aging via Mitochondria-associated Neuroinflammation

Xifei YANG

Shenzhen Center for Disease Control and Prevention

Biography:

Xifei YANG studied at Huazhong University of Science and Technology, Hong Kong University, and Harvard University, and received systematic scientific training. Focusing on basic and translational research on neurodegenerative diseases for more than 20 years. He has presided over 15 projects including the National Natural Science Foundation of China youth/general projects, Sino-US international cooperation and exchange projects, etc. He has won a total of 7 items including the National Excellent Youth Science and Technology Award of the Chinese Society of Toxicology and the second prize of the Guangdong Science and Technology Award. Presided over the preclinical drug efficacy evaluation of 3 new class 1 new drugs, of which 1 ALS project was approved by the State Food and Drug Administration to enter phase II clinical trials (MP-2019-004/CXHL2000169) and US FDA clinical trial approval, 1 Al The Alzheimer's disease drug project was approved by the National Clinical Trial License (2021LP01705). Published 128 SCI papers in journals such as *Signal Transduct Target Ther* (IF=38.104), *Theranostics* (IF=11.6), *Aging Cell* (IF=11.005), *J Clin Invest* (IF=19.456), among which the corresponding or co-corresponding authors published IF10 10 papers. Guiding/cooperating to guide 42 masters, doctors and postdoctoral fellows. Editorial board member of Front Neurosci (Switzerland) and Am J Alzheimers Dis Other Demen (USA).

Abstract:

Background: A wide spectrum of changes occurs in the brain with age, from molecular to morphological aspects, and inflammation accompanied by mitochondria dysfunction is one of the significant factors associated with age. Adiponectin (APN), an essential adipokine in glucose and lipid metabolism, is involved in the aging; however, its role in brain aging has not been adequately explored. Here, we aimed to explore the relationship between APN deficiency and brain aging using multiple biochemical and pharmacological methods to probe APN in humans, KO mice, primary microglia, and BV2 cells. Results: We found that declining APN levels in aged human subjects correlated with dysregulated cytokine levels, while APN KO mice exhibited accelerated aging accompanied by learning and memory deficits, anxiety-like behaviours, neuroinflammation, and immunosenescence. APN-deficient mice displayed aggravated mitochondrial dysfunction and HDAC1 upregulation. In BV2 cells, the APN receptor agonist AdipoRon alleviated the mitochondrial deficits and aging markers induced by rotenone or antimycin A. HDAC1 antagonism by Compound 60 (Cpd 60) improved mitochondrial dysfunction and age-related inflammation, as validated in D-galactose-treated APN KO mice.

Conclusion: Altogether, these findings indicate that APN is a critical regulator of brain aging by preventing neuroinflammation associated with mitochondrial impairment via HDAC1 signalling. Keywords: Adiponectin, Aging, HDAC1, Neuroinflammation, Mitochondria, BV2 Cells.

Effect of Vestibular Dysfunction on Cognition

Haiwei HUANG

Sun Yat-Sen University

Biography:

Haiwei Huang is the professor of First Affiliated Hospital of Sun Yat-sen University as well as the executive chairman and secretary general of South China Vertigo Center Alliance. He is committed to the mechanism and objective evaluation of vestibular balance dysfunction and cognitive impairment, basic research on radiation brain injury and vestibular dysfunction, undertook many projects such as National Natural Science Foundation, Guangdong Provincial Science and Technology Plan and Guangzhou Municipal Science and Technology Plan, and published many related papers as the first author or communication author.

Abstract:

Previously, it was believed that vestibular input and its pathways were involved in spatial orientation and balance regulation, but more and more research has found that vestibular dysfunction may also have an impact on cognition, including visual spatial ability, memory, attention, and executive ability. This speech will provide a detailed introduction to the impact of unilateral vestibular dysfunction, vestibular migraine, bilateral vestibular disease, and persistent posture perception dizziness on cognitive function, as well as the strategies we can adopt. In addition, we have also proposed key points to pay attention to in clinical practice for the elderly and children.

Hypochlorous Acid Derived from Microglial Myeloperoxidase Mediates High-mobility Group Box 1 Release from Neurons to Amplify Brain Damage in Cerebral Ischemia-reperfusion Injury

Jiangang SHEN

The University of Hong Kong

Biography:

Dr. Shen Jiangang is Professor and Chairman, Department Research Postgraduate Committee, School of Chinese Medicine and Principal Inverstigator, State Key Laboratory of Pharmaceutical Biotechnology, University of Hong Kong. Dr. Shen's research focuses on oxidative and redox signalling for brain damage and neurological functional repair in post stroke and application for drug discovery. He has published 175 SCI papers in prestigious international academic journals and over 60 Chinese academic papers. He has also published 19 books or book chapters and filed 10 patents.

Abstract:

Myeloperoxidase (MPO) plays critical role in the pathology of cerebral ischemia-reperfusion (I/R) injury via producing hypochlorous acid (HOCl) and inducing oxidative modification of proteins. High-mobility group box 1 (HMGB1) oxidation, particularly disulfide HMGB1 formation, facilitates the secretion and release of HMGB1 and activates neuroinflammation, aggravating cerebral I/R injury. However, the cellular sources of MPO/HOCl in ischemic brain injury are unclear yet. Whether HOCl could promote HMGB1 secretion and release remains unknown. In the present study, we investigated the roles of microglia-derived MPO/HOCl in mediating HMGB1 translocation and secretion, and aggravating the blood-brain barrier (BBB) disruption and brain damage in cerebral I/R injury. *In vitro*, under the co-culture condition with microglia BV cells but not the single culture condition, oxygen-glucose deprivation/reoxygenation (OGD/R) significantly increased MPO/HOCl expression in PC12 cells. Exposure to OGD/R, MPO-containing exosomes derived from BV2 cells were released and transferred to PC12 cells, increasing MPO/HOCl in the PC12 cells. The HOCl promoted disulfide HMGB1 translocation and secretion and aggravated OGD/R-induced apoptosis. *In vivo*, SD rats were subjected to 2 h of middle cerebral artery occlusion (MCAO) plus different periods of reperfusion. Increased HOCl production was observed at the reperfusion stage which was accomplished with enlarged infarct volume, aggravated BBB disruption and neurological dysfunctions. Treatment of MPO inhibitor 4-aminobenzoic acid hydrazide (4-ABAH) and HOCl scavenger taurine reversed those changes. HOCl was colocalized with cytoplasm transferred HMGB1, which was blocked by taurine in rat I/R-injured brain. We finally performed a clinical investigation and found that plasma HOCl concentration was positively correlated with infarct volume and neurological deficit scores in ischemic stroke patients. Taken together, we conclude that ischemia/hypoxia could activate microglia to release MPO-containing exosomes that transfer MPO to adjacent cells for HOCl production; Subsequently, the production of HOCl could mediate the translocation and secretion of disulfide HMGB1 that aggravates cerebral I/R injury. Furthermore, plasma HOCl level could be a novel biomarker for indexing brain damage in ischemic stroke patients.

Plenary Session TWO

Session Chair: Chuxia DENG
Session Co-Chair: Han Ming SHEN

Creating Paradigms Shift in Molecular Diagnostics

Dennis LO

The Chinese University of Hong Kong

Biography:

Professor Dennis Lo is the Associate Dean (Research) of the Faculty of Medicine of The Chinese University of Hong Kong, and the President of Hong Kong Academy of Sciences. His research interests focus on the biology and diagnostic applications of cell-free nucleic acids in plasma. In particular, he discovered the presence of cell-free fetal DNA in maternal plasma in 1997 and has since then been pioneering non-invasive prenatal diagnosis using this technology. This technology has been adopted globally and has created a paradigm in prenatal medicine. He has also made many innovations using circulating nucleic acids for cancer detection, including the screening of early stage nasopharyngeal cancer. In recognition of his research, Professor Lo has been elected as Fellow of the Royal Society, Foreign Associate of the US National Academy of Sciences, Fellow of The World Academy of Sciences (TWAS) and Founding Member of the Academy of Sciences of Hong Kong. Professor Lo has won numerous awards, including the 2014 King Faisal International Prize in Medicine, the 2016 Future Science Prize in Life Science, the 2019 Fudan-Zhongzhi Science Award, the 2021 Breakthrough Prize in Life Sciences, the 2021 Royal Medal, the 2021 ESHG Mendel Award, the 2022 ISPD Pioneer Award and the 2022 Lasker~DeBakey Clinical Medical Research Award.

Abstract:

TBC

A Temporal Signaling Code to Specify Immune Responses

Alexander HOFFMANN

University of California, Los Angeles

Biography:

Alexander Hoffmann is the Thomas M Asher Professor of Microbiology and Immunology at UCLA, and the founding director of the Institute for Quantitative and Computational Biosciences (QCBio). His research aims to develop a predictive understanding of immune responses, focusing on immune sentinel macrophages, on the generation of antibody responses by B-cells, and on the impact of immune responses on the generation of new immune cells via hematopoiesis. Before joining UCLA in 2014, he was Professor of Biochemistry at UCSD; there he founded the San Diego Center for Systems Biology (SDCSB), co-founded the BioCircuits Institute (BCI), and directed the Graduate Program in Bioinformatics and Systems Biology. He holds degrees in Physics and Zoology (BA, Cambridge University), Biochemistry and Molecular Biology (PhD, Rockefeller University) and owes his training to Robert Roeder and David Baltimore, as well as his many students, postdocs and collaborators.

Abstract:

Immune sentinel cells such as macrophages survey the tissue microenvironment and must initiate the appropriate immune response upon sensing the presence of diverse pathogens or immune threats. Indeed, macrophages are capable of stimulus-specific responses, but a very large number of receptors utilize only a handful of signaling pathways. Interestingly, the downstream transcription factors exhibit complex dynamics, which in turn determine which genes are activated. I will discuss our recent studies to determine whether these dynamics represent a signaling code or language that may specify the immune responses of immune sentinel cells. I will present recent work in which we were able to identify the “words” of this language, and characterize their reliability and points of confusion. I will then discuss how immune response genes interpret these "words" to generate an appropriate immune response.

Diverse Nuclear Factors are Enablers of NF-κB's Transcriptional Activity

Gourisankar GHOSH

University of California San Diego

Biography:

I earned my undergraduate and master degrees at Calcutta University, India, before moving to the USA to pursue my PhD I worked under Professor LaDonne Schulman and completed my PhD in 1990. I moved to Yale University to conduct postdoctoral research under Professor Paul Sigler. As a graduate student, I used biochemical and molecular methods to study translational regulation. As a postdoctoral researcher, I switched to studying transcriptional control using X-ray crystallography. I moved to UC San Diego as an Assistant Professor in 1995 and continued my research to understand the structural mechanism of gene regulation by the NF-kappaB family of transcription factors. I subsequently expanded my research program into pre-mRNA splicing. Very recently, I have been involved in aging research with a particular emphasis on neurological diseases such as Alzheimer's disease. The central theme of my research is how deregulation of NF-kappaB activity leads to persistent inflammation and pathogenic consequences.

Abstract:

I will describe how RelA, a member of the NF-kappaB family of transcription factors, activates gene transcription by binding to a large variety of promoters that contain multiple binding sites known as kappaB sites. RelA alone is unable to mediate transcription and requires other nuclear factors, including other DNA binding transcription factors, transcriptional co-regulators, RNA binding proteins and enzymes. Many of these factors bind kappaB sites for binding.

Liquid–liquid Phase Separation in Autophagy

Hong ZHANG

Institute of Biophysics, Chinese Academy of Sciences

Biography:

Dr. Hong Zhang is an Investigator in the Institute of Biophysics, Chinese Academy of Sciences. Zhang's lab demonstrated that during *C. elegans* embryogenesis, specialized protein aggregates, called PGL granules, are removed by autophagy in somatic cells. Using this as a model, his lab carried out the first systematic genetic screens in multicellular organisms and identified a set of metazoan-specific autophagy genes, called Epg genes. His lab further revealed that Epg genes act at steps unique to the autophagy pathway in multicellular organisms. Currently, the research in Zhang's lab focuses on phase separation of autophagy proteins and regulators in various aspects of autophagy, including execution and regulation of autophagy and also degradation of protein aggregates. The awards he has won in recent years include the Second Prize of The State Natural Science Award, the 6th C.C.Tan Life Science Award, National Outstanding Young Scientist Award, and an HHMI International Early Career Scientist Award. Dr. Hong Zhang is an Associate Editor for Autophagy and is also on the *Editorial Board for Trends in Biochemical Sciences, Journal of Cell Biology, eLife, EMBO reports, JCS and Cell Death & Differentiation*.

Abstract:

Autophagy involves the enclosure of cytoplasmic material in the autophagosome and its subsequent delivery to the lysosome for degradation and recycling. A long-standing unanswered question in autophagy concerns the identity of the signal that initiates autophagosome formation on the ER in multicellular organisms. We demonstrated that autophagy stimuli trigger Ca2+ transients/oscillations on the outer surface of the ER membrane, whose amplitude, frequency and duration are controlled by the metazoan-specific ER transmembrane autophagy protein EPG4/EI24. Ca2+ transients trigger liquid-liquid phase separation of the autophagosome-initiating FIP200 complex. The liquid-like FIP200 condensates associate with the ER via interacting with the ER transmembrane proteins VAPA/B and ATL2/3, and further assemble into autophagosome formation sites. Our study reveals a crucial role of Ca2+ transients at the ER/cytosol interface in triggering LLPS of FIP200 for specification of autophagosome initiation sites in multicellular organisms.

Mitochondria Quality Control and Parkinson's Disease

Richard J. YOULE

National Institute of Neurological Disorders and Stroke,
National Institutes of Health

Biography:

Dr. Youle received an A.B. degree from Albion College and his PhD degree from the University of South Carolina where he worked on the protein toxin ricin. He joined the lab of David Neville at the National Institute of Mental Health for postdoctoral work on engineering new cell-type-specific protein toxins. He joined the Surgical Neurology Branch of NINDS in 1985 as a principal investigator where he has developed and moved into clinical trials new treatment strategies for brain tumours. His lab subsequently explored the molecular mechanisms of programmed cell death showing how Bcl-2 family members participate with mitochondria to control cell survival. Most recently his lab has discovered functions and interrelationships among proteins mutated in familial Parkinson's disease. His current work focuses on molecular mechanisms of autophagy, mitochondrial quality control and neurodegenerative disorders.

Abstract:

TBC

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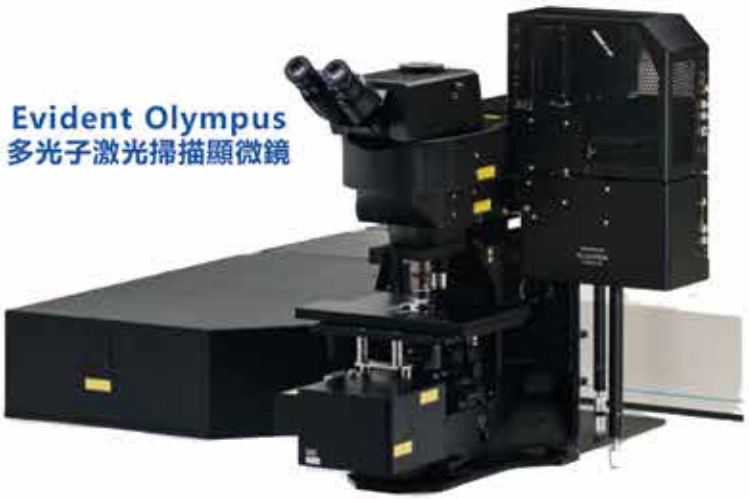

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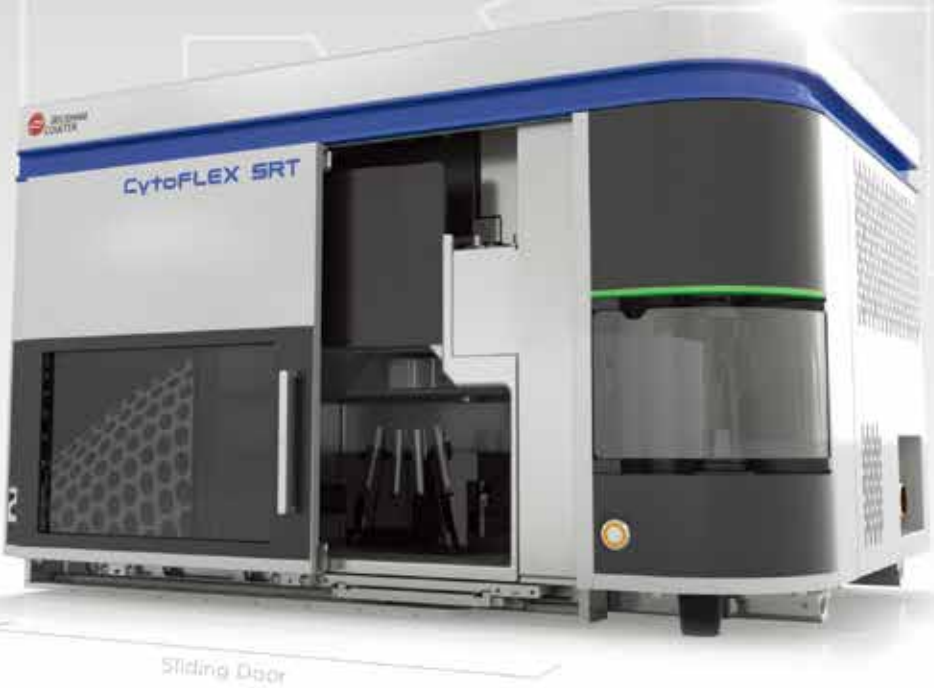

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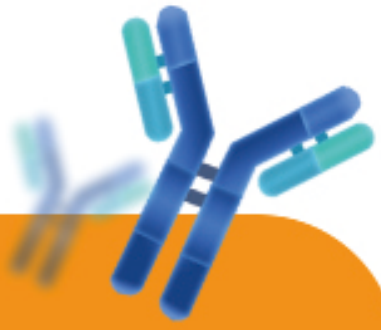

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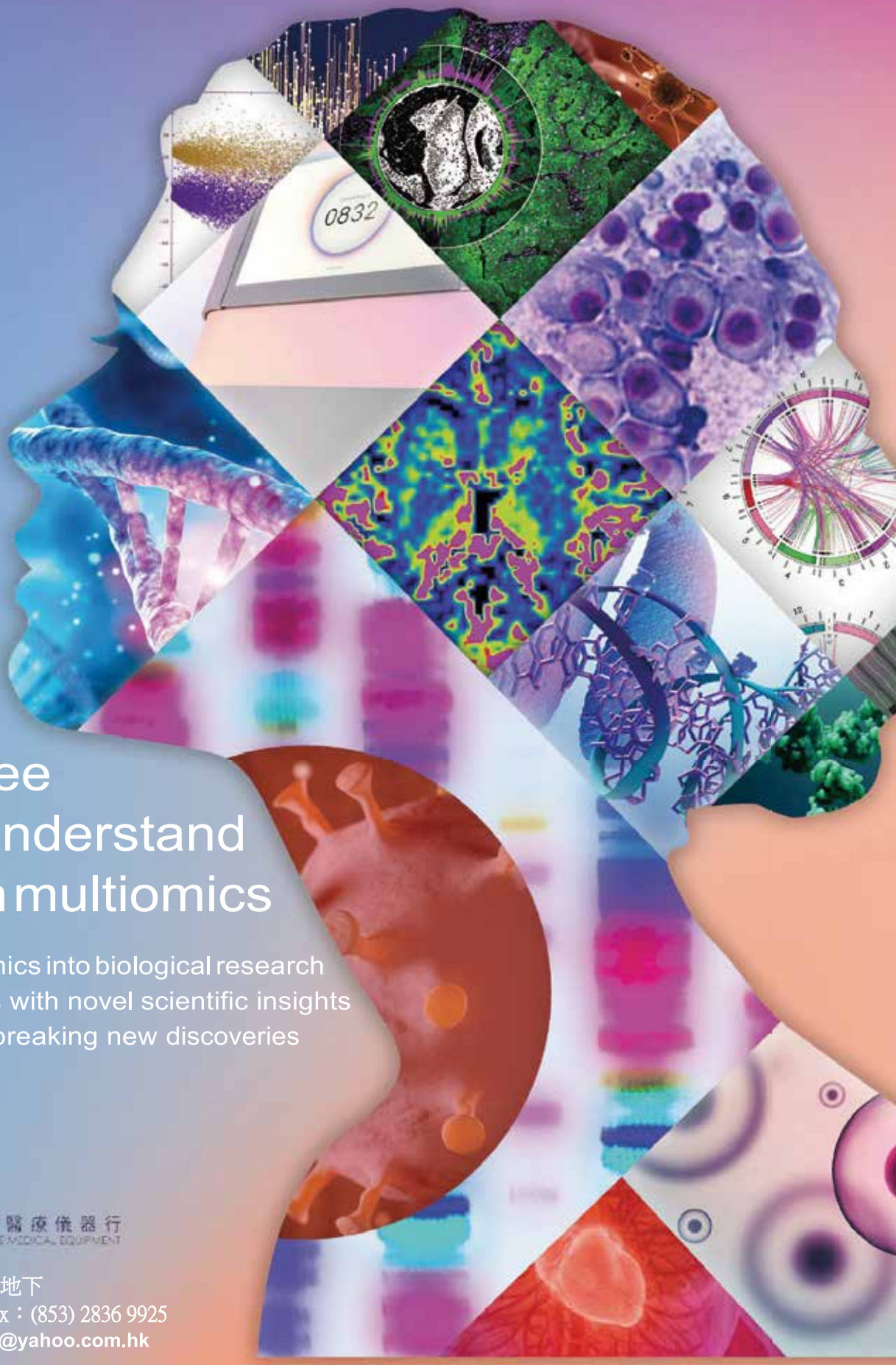

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