11th MACAU SYMPOSIUM ON BIOMEDICAL SCIENCES

SCIENTIFIC IMPACT

20-21 June 2025

Organizer

澳門大學
UNIVERSIDADE DE MACAU
UNIVERSITY OF MACAU

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Faculty of Health Sciences

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	Programme Introduction - **Chuxia DENG** Dean, Faculty of Health Sciences, University of Macau
	Group Photo

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10:30 - 13:00	**Xin LU**, University of Oxford Infection, Cell Plasticity and Upper GI Cancers
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21 June, Saturday - AM

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13:00 - 14:30	Luncheon (Venue: N1-G006 Grand Plaza, by invitation)

21 June, Saturday - PM

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21 June, Saturday - PM

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	Zhuo SHANG, Shandong University Mandimycin: A New Polyene Macrolide Antifungal with a Unique Mode of Action
	Ningning LIU, Shanghai Jiao Tong University Fungi and Cancer: From Gut to Intratumour
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Best Poster Awards Presentation
Closing Ceremony of
the 11th Macau Symposium on Biomedical Sciences

18:00 - 18:30	Presentation of Selected Posters
	Best Poster Awards
	Closing Ceremony - **Ren-He XU** Associate Dean (Research), Faculty of Health Sciences, University of Macau

- The End -

Faculty of Health Sciences, University of Macau

With the vigorous support and joint efforts from numerous supporters, the Faculty of Health Sciences (FHS) of the University of Macau (UM) has thrived since its establishment in 2013. As a fundamental academic unit, FHS, comprised of three departments (Department of Biomedical Sciences, Department of Pharmaceutical Sciences and Department of Public Health and Medicinal Administration), now offers three undergraduate programmes, two master programmes and two doctoral programmes. The programmes are delivered by an excellent team of academics who have guided and inspired over 750 young researchers and students in the lifelong quest of knowledge.

The research of FHS focuses on ten major themes, they are: (i) Precision Oncology, (ii) Stem Cell and Development (iii) Aging, Neural and Metabolism Disorders and Infectious Diseases, (iv) Biomedical Imaging, (v) Data Science, (vi) Drug Development, (vii) Neuropsychiatry, (viii) Structural Biology, (ix) Translational Medicine and x) Public Health. To support these research activities, FHS has established a state-of-the-art infrastructure that includes more than 40 research laboratories, 4 research centres and 4 core facilities. In addition, upon the approval of the Ministry of Education, UM established the first Frontiers Science Center in Hong Kong and Macao in 2021, namely “Frontiers Science Center for Precision Oncology”, which is formed a team led by FHS, dedicating to carry out cutting-edge scientific research of common cancers in Macao. In addition, FHS initiated abundant projects as the principle unit, one of which is a National Key R&D Programme of China to support a multi-institutional project on stem cell therapy.

With this solid research support, FHS has recorded a steady increase in the quantity and quality of publications and scientific discoveries in the past decade. The accumulative number of papers published by FHS scholars increased from 43 in 2014 to over 2,400 in June 2025, with over 68,000 citations and over 400 accumulative publications with impact factor ≥10. The success and impact of FHS in research are also shown by the fact that health sciences-related subjects of UM, including Biology and Biochemistry, Chemistry, Clinical Medicine, Pharmacology and Toxicology, Psychiatry/Psychology, Molecular Biology and Genetics have entered top 1% rank of the Essential Science Indicators (ESI). Besides, UM is ranked No. 180 in the Times Higher Education (THE) World University Rankings 2025 and 151-175 bracket in the subject ‘Medical and Health’ and ‘Life Sciences’, recognising the important and sustained contributions of FHS in related research areas.

These research output signifies the continual improvement in the overall influence worldwide of FHS in health sciences. Equally important, FHS has organised numerous symposia and seminars including Macau Symposium on Biomedical Sciences (MSBS) and International Conference of the Greater Bay Area on Regenerative Medicine (GBRM) to deliver talks with topics both in cutting-edge science and popular science, and assisted local schools in devising and operating STEM education programmes, all of which benefit the general understanding of biomedical science and health sciences by the community.

https://fhs.um.edu.mo/

11th Macau Symposium on Biomedical Sciences

Session

Session Chairs:

Chuxia DENG, Ren-He XU

Plenary Session

AIEgens: Conceptually New Bioprobes for Visualizing Biostructures and Monitoring Bioprocesses

Ben Zhong TANG

Dean of School of Science and Engineering and
X.Q. Deng Presidential Chair Professor
The Chinese University of Hong Kong, Shenzhen

Biography:

Prof Tang received his BS and PhD degrees from South China University of Technology and Kyoto University in 1982 and 1988, respectively. He conducted postdoctoral research at The University of Toronto from 1989 to 1994. He joined the Hong Kong University of Science & Technology in 1994 and was promoted to Chair Professor in 2008. He was elected to the Chinese Academy of Sciences in 2009 and the World Academy of Sciences for the Advancement of Science in Developing Countries in 2020. In 2021, he joined The Chinese University of Hong Kong, Shenzhen, as Dean of School of Science and Engineering, with a concurrent appointment of X.Q. Deng Presidential Chair Professor. Prof Tang has published >2,000 scientific papers, which have been cited >223,320 times. His h-index is 207. He has delivered >500 invited talks at international conferences and has been granted >100 patents. He is currently serving as Editor-in-Chief of Aggregate published by Wiley, and is sitting in the editorial boards of >20 scientific journals. Prof Tang is mainly engaged in the study of materials science, macromolecular chemistry and biomedical theranostics. He coined the concept of aggregation-induced emission (AIE), and his labs are spearheading the AIE research in the world. Prof Tang has been listed as a Highly Cited Researcher in both areas of Chemistry and Materials Science since 2014. He received a series of awards, scholarships and honours, e.g., Croucher Senior Research Fellowship Award in 2007, Honorary Citizen of Guangzhou City in 2015, National Natural Science Award (1st Class) in 2017, Scientific and Technological Progress Award (Ho Leung Ho Lee Foundation) in 2017, Nano Today Award in 2021, Biomaterials Global Impact Award in 2023, and CCS-SINOPEC Award(the Chinese Chemical Society) in 2024.

Abstract:

Advanced bioprobes are highly demanded for biomedical research and theranostic applications. Fluorescence is useful for *in situ* visualization of biostructures and real-time monitoring of bioprocesses. The fluorescence from conventional organic dyes is often weakened in the aggregate state, leading to the aggregation-caused quenching (ACQ) effect. They have developed a conceptually new anti-ACQ system, where the fluorogens are almost non-fluorescent when molecularly dissolved but become highly emissive when nanoscopically aggregated. This effect is named aggregation-induced emission (AIE). With their remarkable advantages of high emission efficiency, low background noise, excellent photostability and large Stokes' shift, the fluorogens with AIE attribute(AIEgens) have been utilized as new bioprobes. In this talk, he illustrates the biomedical applications of the AIEgens for *in vitro* sensing and imaging and *in vivo* diagnostics and therapy.

Infection, Cell Plasticity and Upper GI Cancers

Xin LU

Director of Ludwig Institute for Cancer Research
University of Oxford

Biography:

Prof Lu is Director of the Ludwig Institute for Cancer Research and Professor of Cancer Biology at the University of Oxford, UK. She is a leading cancer cell biologist with long-standing research interests in tumour suppression. She was one of the first researchers to show that the tumour suppressor p53 responds to both oncogene activation and DNA damaging signals and her group was also among the first to demonstrate how to selectively activate p53 to kill cancer cells, through identification and characterization of the evolutionarily conserved ASPP family of proteins. Her laboratory has broad interests in the molecular mechanisms that control cellular plasticity, including how external signals- such as infection- are integrated into the nucleus to achieve target-selective transcription and cell fate determination. Prof Lu also has interests in the deep phenotyping clinical cohorts at high risk of cancer, with an aim to identifying biomarkers and signatures predictive of early stage cancer or recurrence. She is involved in clinical studies on Li Fraumeni Syndrome, Barrett's oesophagus, and played a leading role in the LUD2015-005 Phase II/III immunochemotherapy oesophageal cancer trial, which identified a novel gene signature and tumour monocyte content as independent predictors of patient response. Prof Lu has been elected as a Fellow of the Royal Society 2020, the UK's distinguished academy of science, for her contributions to cancer biology. She is also a Member of the Academy of Medical Sciences, a Member by election of the Academia Europaea, and a Member of the European Molecular Biology Organisation. She is Cancer Theme Leader for the National Institute for Health Research(NIHR) Oxford Biomedical Research Centre and Director of the Oxford Centre for Early Cancer Detection. She has a BSc from Sichuan University, MSc from Peking Union Medical College, Chinese Academy of Medical Sciences in China, PhD from University College London(UCL) and the former Imperial Cancer Research Fund, and postdoctoral training at Dundee University, UK. She was appointed as the Director of Ludwig Institute in London at UCL in 2004 and she established Ludwig Oxford as Director in 2007.

Around 20% of human cancers are attributed to known cancer causing pathogens including EBV, HPV, HBV, and *H. Pylori* and the number is increasing with new discoveries of previously unrecognised cancer-causing pathogens. The most known oncogenic properties of cancer-causing pathogens are their abilities to disrupt the host genome and alter cell plasticity of the infected cells. Bacteria *H. Pylori* is known to cause gastric cancers and the oncoprotein of CagA is a potent inducer of cell plasticity changes such as epithelial to mesenchymal transition (EMT). EBV also associates with a unique gastric cancer subtype. Therefore, a deep understanding of pathogen-host interactions and harnessing host immunity to selectively eliminate tumour virus infected cancers could benefit millions of patients. One of the main research focuses of her group is to identify and characterize the molecular switches of cell plasticity-the ability of cells to change their characteristics and fate. Cell plasticity is a key feature of development, regeneration and cancer and it plays key roles in the development and progression of upper GI (esophageal and gastric) cancers. They revisited the role of cancer-causing pathogens, such as *H. Pylori* and EBV on their ability to control the cell plasticity of host cells and vice versa. They have also focused their studies on human Barrett's oesophagus and oesophageal adenocarcinoma, well-known human conditions in which cell plasticity control is dysfunctional. Immunochemotherapy is now a first line cancer therapy, but the key challenge is to understand why some patients achieve clinical benefit whereas others do not. She discusses the details of their uniquely designed window-of-opportunity trial (LUD2015-005), in which 35 inoperable oesophageal adenocarcinoma (OAC) patients received first-line immune checkpoint inhibitor (ICI) for four weeks (ICI-4W), followed by immunochemotherapy (ICI+CTX). Comprehensive biomarker profiling was conducted, including generation of a 65,000-cell single-cell transcriptomic atlas of oesophageal cancer, as well as multi-timepoint transcriptomic profiling of OAC during ICI-4W, revealing a novel T-cell inflammation signature (INCITE) whose upregulation correlated with ICI-induced tumour shrinkage. Deconvolution of pre-treatment gastro-esophageal transcriptomes using their single-cell atlas identified high tumour monocyte content (TMC) as an unexpected ICI+CTX-specific predictor of greater overall survival (OS) in LUD2015-005 patients, and of ICI response in an independent cohort of selected gastric cancer subtypes. Tumour mutational burden was an additional independent and additive predictor of LUD2015-005 OS. TMC can improve patient selection for emerging ICI+CTX therapies in gastro-esophageal cancer.

Fibroblastic Reticular Cells Control Immune Cell Activity and Interaction

Burkhard LUDEWIG

Head of Medical Research Center
Cantonal Hospital St. Gallen

Biography:

Prof Burkhard LUDEWIG is heading the Medical Research Center at the Cantonal Hospital St. Gallen, Switzerland, and the Translational Cardioimmunology Unit at the University Hospital Zurich, Switzerland. His research is focused on the interaction of stromal cells with innate and adaptive immune cells. They have established preclinical models to study stromal cell function and have developed TCR transgenic mouse models to study viral infection and autoimmune myocarditis. Their clinical research program is focused on myocardial inflammatory diseases.

Abstract:

Fibroblastic reticular cells (FRCs) are specialized fibroblasts of secondary lymphoid organs that provide the structural foundation of the tissue. Moreover, FRCs guide immune cells to dedicated microenvironmental niches where they provide lymphocytes and myeloid cells with homeostatic growth and differentiation factors. Inflammatory processes induce rapid morphological and functional adaptations that are critical for the priming and regulation of protective immune responses. In this presentation, he presents their recent findings on molecular pathways that regulate FRC-immune cell crosstalk in specialized niches during the generation of protective immune responses in infection, cancer and autoimmune disease.

Membrane Atg8ylation and Its Manifestations

Vojo Peter DERETIC

Professor and Chair
University of New Mexico

Biography:

Prof Deretic, PhD, is the director of the NIH-funded Autophagy, Inflammation and Metabolism (AIM) Center of Biomedical Research Excellence. The AIM center aims to promote autophagy research nationally and internationally as well as to develop a cadre of junior faculty along with senior experts in this area to study fundamental mechanisms and how autophagy intersects with a broad spectrum of human disease and health states. Prof Deretic is the departmental chair of the Department of Molecular Genetics and Microbiology at the University of New Mexico School of Medicine. He received his undergraduate, graduate and postdoctoral education in Belgrade, Paris, and Chicago. Prof Deretic's main contributions to science come from studies by his team on the role of autophagy in homeostatic processes with additional emphasis on its immunological functions. Recently, his group has uncovered previously unappreciated roles of small ubiquitin-like molecules known as mATG8s and defined the more general principle of 'membrane atg8ylation' of which canonical autophagy is only one of its biological outputs.

Abstract:

Membrane atg8ylation represents a paradigm shift in our understanding of the molecular machinery previously thought to be exclusively involved in autophagy. There are multiple biological outputs of membrane atg8ylation, of which canonical autophagy is just one of its manifestations. In principle, membrane atg8ylation is a newly recognized general process of membrane homeostasis and remodeling, functioning on cellular membranes akin to how ubiquitin works with proteins. The focus of this talk is to introduce this novel cell biological process, present its fundamental principles and mechanisms, and illustrate the breath of its varied physiological manifestations that are only beginning to be appreciated.

Novel CAR-T Cellular Therapy for Hematological Malignancies

He HUANG

Director of Bone Marrow Transplantation Center
Zhejiang University

Biography:

Prof Huang, MD, PhD, Director of Bone Marrow Transplantation Center of The First Affiliated Hospital, Zhejiang University School of Medicine; Director of Hematology Institution of Zhejiang University. Prof Huang is also actively involved in and holds key positions in a number of professional organizations and scientific committees, including being Vice Chairman of Experts Committee of Chinese Marrow Donor Program; Executive Committee Member of Asia-Pacific Bone Marrow Transplantation Group (APBMT); Committee member of European Society of Hematology (EBMT); Vice President of Asian Cellular Therapy Organization (ACTO). Prof Huang specializes in clinical and basic research on hematopoietic stem cell transplantation, cellular immunotherapy and stem cell biology research. He created an integrated treatment system of CAR-T cell therapy combined with haploidentical hematopoietic stem cell transplantation for refractory/recurrent malignant hematological diseases. As corresponding author, he has published 278 original papers in SCI-cited journals including *New England Journal of Medicine*, *Nature*, *Cell Research*, *Lancet Haematology*, *Cell Metabolism* etc.

Abstract:

Chimeric antigen receptor(CAR) T-cell therapies have achieved remarkable success in the treatment of haematological malignancies. In recent years, the use of CAR-T cell therapies has expanded throughout China, from the first CAR-T cell clinical trial conducted in 2013, to the world's largest number of CAR-T cell-related clinical trials by 2017, to a cumulative $2.37 billion in funding for cell therapy companies in 2021, and a significant growth in the number of CAR T-cell-related clinical trials and basic researcher. This strong uptick in activity is the result of a culmination of China-unique factors: strong government support, capital inflow, large patient demand, a unique healthcare system and the great efforts of Chinese scientists. This report provides an overview of the current scope of CAR-T cell clinical trials in China, analyzes the relevant policies, and sorts out the achievements and challenges of CAR-T cell therapy in China to provide a better understanding for further promoting cellular therapy development and clinical application. Novel CAR-T cells including novel targets, enhanced function, precise regulation and universal CAR-T cells are introduced.

Decoding TGF-β's Paradox in Cancer

Xinhua FENG

Qiushi Chair Professor and
Director of Life Sciences Institute
Zhejiang University

Biography:

Prof Feng is the Qiushi Chair Professor and Director of the Life Sciences Institute at Zhejiang University. He earned his BS from Wuhan University, MS from the Institute of Genetics at the Chinese Academy of Sciences, and PhD from the University of Maryland-College Park. After completing postdoctoral training at the University of California-San Francisco, he moved through the ranks at Baylor College of Medicine, becoming a tenure-track assistant professor, then associate and full professor. Since 2009, he has founded the Life Sciences Institute at Zhejiang University. His research focuses on unraveling the mechanisms and interactions among protein modifications, signaling pathways, and gene transcription in development and disease. Current projects include investigating the TGF-β/BMP signaling network, understanding mechanisms by which cancer evades anti-growth control, studying noncoding RNAs and RNA-binding proteins in cancer progression, and exploring lysosomal functions and storage disorders, ultimately aimed at developing improved therapeutics.

Abstract:

Members of TGF-β superfamily play essential roles in normal development. In physiological settings, strength and duration of TGF-β signaling are tightly and precisely controlled. Dysregulation or dysfunction of TGF-β signaling is associated with pathogenesis of human diseases. For instance, loss of the TGF-β antiproliferative response is a hallmark in human cancers. Tumour cells have developed a number of strategies to escape from negative growth control. One major mechanism to resist the cytostatic effect of TGF-β is through inactivating mutations/deletions in the TGF-β signaling pathway, which frequently occur in gastrointestinal and pancreatic cancer. For example, tumour suppressor Smad4/DPC4, the central transducer of TGF-β signaling, is deleted in more than half of pancreatic cancer patients. However, deletion or mutations in the Smad4 gene are rare in other types of cancers. They have taken functional genomic, proteomic and cell biological approaches to study how the tumour suppressor function is regulated in normal and cancer cells. They have found that activation of many oncoproteins can cause cellular resistance to TGF-β growth inhibitory function, and/or amplify TGF-β metastasis-promoting functions. Their novel studies gain conceptual insights into the oncoprotein-tumour suppressor interplay in tumorigenesis and provide guidance to logical therapeutic designs in cancer prevention, diagnostics and treatment.

11th Macau Symposium on Biomedical Sciences

Session I

Session Chairs:

Edwin CHEUNG, Qihan CHEN

Genome Biology

Precise RNA Targeting and Intervention

Chengqi YI

Boya Distinguished Professor
Peking University

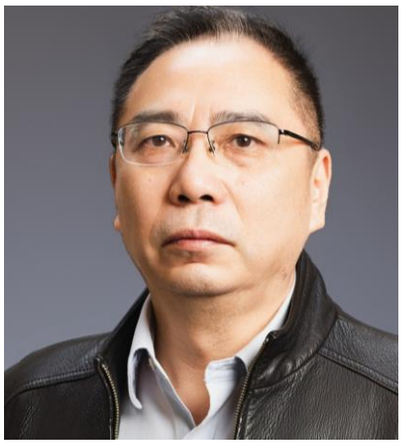
Biography:

Prof Yi is a Boya Professor at School of Life Sciences at Peking University. He is also a Senior Investigator at Peking-Tsinghua Center for Life Sciences, and holds a joint professorship at College of Chemistry and Molecular Engineering at PKU. The Yi Lab studies RNA modifications and their roles in gene expression regulation. In particular, they focus on the regulation and functions of non-m6A RNA modifications, including pseudouridine (4), N1-methyladenosine (m1A) and N6,2-O'-dimethyladenosine (m6Am). Their findings add to the expanding repertoire of mRNA modifications and open up new directions of post-transcriptional modifications and epitranscriptomics. A second field that interests him is genome editing. Combining their expertise in chemical biology and genomics, the Yi Lab has developed multiple sequencing technologies to investigate the off-target editome of DNA base editors. Based on such understanding, they then developed new tools that are more precise and efficient.

Abstract:

Nonsense mutations, responsible for ~11% of genetic diseases, create premature termination codons (PTCs) and lead to truncated and often non-functional proteins. Recently, programmable RNA pseudouridylation has emerged as a new type of RNA base editor to suppress PTCs. However, current methods suffer from low efficiency and limited precision. Here they develop RESTART v3, an updated version of RESTART, which utilizes near-cognate tRNAs to improve the readthrough efficiency of pseudouridine-modified PTCs. They show an average of ~5-fold higher editing efficiency than RESTART v2 in cultured cells, currently the most active RNA pseudouridylation tool to mediate PTC readthrough. Moreover, RESTART v3 achieves functional PTC readthrough in disease cell models of cystic fibrosis and Hurler syndrome. Furthermore, RESTART v3 enables accurate incorporation of the original amino acid for nearly half of the PTC sites, considering the naturally occurring frequencies of sense to nonsense codons. In line with the benign off-target effect of RESTART, RESTART v3 does not change the coding information nor the expression level of transcripts with off-target editing; it does not alter the overall natural tRNA abundance either. Collectively, RESTART v3 represents an enhanced RNA base editor with increased efficiency and accuracy.

SIDT1-Dependent Absorption in the Stomach Mediates Host Uptake of Dietary and Orally Administered MicroRNAs



Chenyu ZHANG

Professor and Dean of School of Life Sciences
Nanjing University

Biography:

Prof Zhang is the pioneer of extracellular microRNA research. In 2007, he has found firstly that the circulating microRNA serves as a novel class of non-invasive biomarker for diseases and can be used to diagnosis, prognosis, etc. In 2010, he has also reported firstly that the secreted microRNA is the novel class of signaling molecule in mediating inter-cellular/inter-organ communication. In 2012, Prof Zhang has reported that functional exogenous plant microRNAs could be absorbed by human and animal. The absorbed exogenous plant microRNA regulated mammalian gene and human and animal's physiology/pathophysiology in a cross-kingdom manner. The current studies will not only discover the roles of ex-RNAs in food/environment affecting human and animal's physiology/pathophysiology, but also find the novel therapeutic strategies to treat diseases. Prof Zhang has published 328 scientific papers. The total citation time is over 61,000 and HI=111. He has also got 53 international patents.

Abstract:

Dietary microRNAs have been shown to be absorbed by mammals and regulate host gene expression, but the absorption mechanism remains unknown. Here, they show that SIDT1 expressed on gastric pit cells in the stomach is required for the absorption of dietary microRNAs. SIDT1-deficient mice show reduced basal levels and impaired dynamic absorption of dietary microRNAs. Notably, they identified the stomach as the primary site for dietary microRNA absorption, which is dramatically attenuated in the stomachs of SIDT1-deficient mice. Mechanistic analyses revealed that the uptake of exogenous microRNAs by gastric pit cells is SIDT1 and low-pH dependent. Furthermore, oral administration of plant-derived miR2911 retards liver fibrosis, and this protective effect was abolished in SIDT1-deficient mice. Their findings reveal a major mechanism underlying the absorption of dietary microRNAs, uncover an unexpected role of the stomach and shed light on developing small RNA therapeutics by oral delivery.

Decode the Human Genome by Epigenetics in Cell-Free DNA and Single-Cells

Yaping LIU

Assistant Professor
Northwestern University Feinberg

Biography:

Prof Yaping LIU is an Assistant Professor (tenure-track) at the Department of Biochemistry and Molecular Genetics in the Northwestern University Feinberg School of Medicine (2023-). He started his lab as an Assistant Professor (tenure-track) at the Division of Human Genetics and Biomedical Informatics at Cincinnati Children's Hospital Medical Center (CCHMC) and the Department of Pediatrics at the University of Cincinnati College of Medicine (2019-2023). Prior to joining CCHMC and UC faculty, he was the principal computational biologist at a liquid biopsy company in 2018. From 2014 to 2017, he was a postdoc associate with Prof Manolis Kellis in the Computer Science and Artificial Intelligence Laboratory at MIT and Broad Institute. In 2014, He received his PhD in Genetics, Molecular and Cellular Biology focused on cancer epigenomics under the supervision of Prof Benjamin P. Berman at the University of Southern California. In 2008, he received his BS in Biotechnology from Nanjing University in China.

Abstract:

His long-term research interest is to decode the human genome. His lab's recent research focus is on developing computational methods for cell-free DNA (cfDNA) and high-throughput experimental methods for single-cell multi-omics. Epigenetic modifications, including DNA methylation, histone modifications, and three-dimensional (3D) genome topology, combine with genetic content to determine the mammalian transcriptional factor (TF) binding and, thus, gene regulation. At present, they are limited by the number of simultaneous measurements that they can perform in the same DNA molecules and single cells. They developed single-cell Methyl-HiC to reveal the heterogeneity of DNA methylation, long-range DNA methylation concordance, and 3D genome in the same cells. Recently, they improved this technology to jointly profile genetic variants, DNA methylation, chromatin accessibility, and 3D genome in the same DNA molecules together with gene expression in the same assay. In cell-free DNA, they developed a set of computational tools to facilitate the study of cellular epigenomes non-invasively by fragmentation patterns measured from cfDNA whole-genome sequencing (WGS). Current research on the development of computational methods for cfDNA fragmentation patterns is significantly limited by the controlled access of the cfDNA WGS. They built and maintained a comprehensive database and browser to host >3,000 uniformly processed and curated de-identified cfDNA WGS for the liquid biopsy community. Further based on the public dataset, they developed a computational method to *de novo* characterize the genome-wide fragmentation hotspots at cfDNA WGS. In healthy, hotspots are enriched in gene-regulatory elements, including open chromatin regions, promoters, and hematopoietic-specific enhancers. The aberration of hotspots detected in early-stage cancers allows them to diagnose early-stage cancers and their tissues of origin with high performance. Recently, they developed a Hidden Markov Model based computational method to accurately predict DNA methylation in the CpG-rich regions and identify the tissues-of-origin in cfDNA from both high-coverage and low-coverage cfDNA WGS. The experimental approaches and computational methods developed for cfDNA fragmentation in their lab will eventually pave the roads for their understanding of the variation of *cis*-regulatory elements non-invasively across different physiological and pathological conditions.

First Generation Spatially-Oriented Maps of Gastric Adenocarcinoma

Boon Ooi Patrick TAN

Professor and Senior Vice Dean (Research)
Duke-NUS Medical School / Cancer Science Institute of Singapore

Biography:

Prof Patrick TAN is Senior Vice Dean (Research) at Duke-NUS Medical School Singapore and Executive Director of PRECISE (Precision Health Research Singapore) coordinating Singapore's National Precision Medicine program. He is also Chief Scientific Officer at the Genome Institute of Singapore, Senior Scientific Advisor (Group Research) at SingHealth, and Professor (adjunct) at Duke University, USA. He received his BA (summa cum laude) from Harvard University and MD PhD degree from Stanford University, where he received the Charles Yanofsky prize. Other awards include the President's Scholarship, Loke Cheng Kim scholarship, Young Scientist Award (A-STAR), Singapore Youth Award, Chen New Investigator Award (Human Genome Organization), President's Science Award, Japanese Cancer Association International Award, Public Administration Medal (Silver), Exemplary Public Service Award, and NUS University Research Recognition Award. He has received the American Association for Cancer Research, Board of Editors for *Science* and *Cancer Discovery*, and on advisory committees for Qatar Precision Health Institute and Riyadh Biotech City (Saudi Arabia).

Abstract:

Tumours are highly dynamic cellular ecosystems where cancer cells engage with other cell types such as immune cells and stromal tissues to promote carcinogenesis and invasion. Interactions between these tumour-resident populations are often sculpted by geospatial context, therapeutic pressure, and organ-site specific metastases. In this talk, he presents a few vignettes describing their attempts to apply spatial transcriptomic technologies to understand the spatial organization of gastric cancer, and how these insights improve their understanding of intra-tumour heterogeneity and mechanisms of gastric malignancy.

Dissecting Cancer Heterogeneity Toward Prevention Strategies

Jin-Xin BEI

Professor
Sun Yat-sen University

Biography:
Prof Bei obtained his BS and PhD degrees from Sun Yat-sen University, Guangzhou, China. Right after that he joined Sun Yat-sen University Cancer Center(SYSUCC) as a postdoc and Genome Institute of Singapore (GIS) as visiting research fellow. He returned to SYSUCC after years of working as research scientist at GIS. His major research interest is to dissect genetic predispositions, acquired alterations, environmental factors (intrinsic and extrinsic) contributing to cancer heterogeneity, as well as the underlying mechanisms. He has published more than 130 scientific papers including those in prestigious journals such as Cell, Nat Genet, Lancet Oncol, etc. He has track-records in organizing large international collaborations.

Abstract:
Cancer patients exhibit a wide range of behaviours in terms of geographic prevalence, clinical presentations, treatment responses, and prognosis. Recent studies indicate that both intrinsic and extrinsic factors shape the tumour microenvironment (TME), influencing cancer development and resulting in heterogenous behaviours. This talk highlights recent advances in decoding the heterogeneous nature of cancer using various omics technologies. It explores how genetic makeup, epigenetic modifications, viral infections, TME components, and their interactions contribute to cancers prevalent in Asia, such as nasopharyngeal carcinoma (NPC) and natural killer T cell lymphoma (NKTCL), which are associated with EBV infection, as well as colorectal cancer. These findings provide insights into biological mechanisms of cancer development and enhanced strategies for risk prediction, patient stratification, and precise treatment, ultimately aiming for more effective cancer prevention.

11th Macau Symposium on Biomedical Sciences

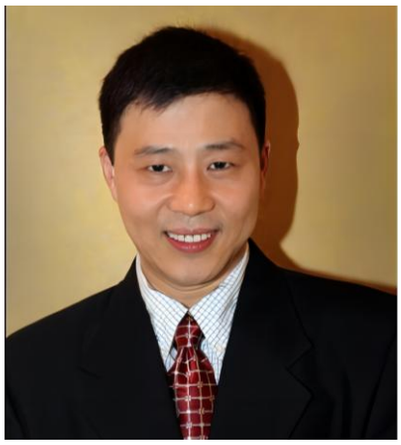
Session II

Session Chairs:

Wenhua ZHENG, Chen MING, Aifang CHENG

Neuroscience, Degenerative Diseases and Aging

Pathogenesis and Early Diagnosis of Neurodegenerative Diseases



Keqiang YE

Chair Professor and Dean
Shenzhen Institute of Advanced Technology
Chinese Academy of Sciences

Biography:

Prof Ye received his undergraduate training in Organic Chemistry at Jilin University(BS, 1990); Graduate training in Polymer Chemistry at Beijing University (MS, 1993); and Graduate training in Biochemistry at Emory University, Atlanta, Georgia, USA (PhD 1998); Postdoctoral training in neuroscience with Prof Solomon H Snyder at Johns Hopkins University (1998-2001). At the end of 2001, he joined the faculty of Emory University, Atlanta, GA, USA (Assistant Professor in Department of Pathology and Laboratory Medicine, 2001-2007; Associate Professor, 2007-2010; Full Professor, 2010-August, 2021). He is now an endowed professor and Dean of Faculty of Life and Health Sciences (FLHS) at Shenzhen University of Advanced Technology (SUAT), Shenzhen, China. Prof Ye is the recipient of numerous professional honors. He has published approximately 300 papers with numerous papers in top journals including: *Cell, Nature*, *Nature Medicine*, *Nature Cell Biology*, *Nature Neuroscience*, *Neuron*, *Mol Cell, EMBO J*, *PNAS* etc. His lab mainly focuses on molecular mechanism in neurodegenerative diseases and drug discovery. He found that AEP acts as a delta-secretase that cleaves both APP and Tau and α-Synuclein, mediating AD/PD pathogenesis. It is an innovative drug target for treating AD and PD. His lab has identified the small molecular inhibitors that display promising therapeutic efficacy toward these neurodegenerative diseases. His lab discoveries support the hypothesis that C/EBPb/AEP signaling acts as a crucial driving factor for neurodegenerative diseases and aging. Moreover, his lab also discovered the first α-Syn PET tracer for PD diagnosis.

Abstract:

Aging is the key risk factor for neurodegenerative diseases. Accumulating evidence suggests that C/EBPb/AEP signalling drives both Alzheimer's disease (AD) and Parkinson's disease (PD) onset and progression. C/EBPb acts as a major transcription factor for AEP (asparagine endopeptidase), and neuronal C/EBPb transgenic mice display gene dose-dependent short lifespan. Deletion of AEP from Thy1-C/EBPb Tg mice extends the lifespan. AEP levels are escalated in the brain in an age-dependent manner, cleaving APP, Tau and α-Synuclein (α-Syn) at N585, N368 and N103, respectively, and triggering Aβ amyloids and Tau aggregation and α-Syn inclusions. Knockout of AEP substantially ameliorates AD and PD pathologies in their mouse models, restoring the behavioral functions. Thus, AEP proteolytic cleavage acts upstream of senile plaques and NFT and Lewy body pathologies, laying foundation for the early diagnosis of these devastating diseases. Quantitative SIMOA (single molecule array) methods have been developed for determining plasma APP N585, C586 and Tau N368 levels. On the other hand, they have developed a small molecular PET tracer that is brain permeable and specifically binds to aggregated α-Syn but not Aβ or Tau in the brains of animal models. [18F]-F0502B recognizes aggregated α-Syn in the non-human primates. Optimization of the lead compound F0502B yields an optimal derivative 6A, which demonstrates desirable PK profiles and displays promising PET imagings for potential clinical application. Early diagnosis of these neurodegenerative diseases will allow us to therapeutically treat or cure these devastating diseases in the future.

APP Is Much More Than An Amyloid Precursor Protein

Karl HERRUP

Professor of Neurobiology
University of Pittsburgh School of Medicine

Biography:

Prof Herrup received his Bachelor's degree from Brandeis University in Waltham, MA, and his PhD in Neuroscience from Stanford University in 1974. After two postdoctoral fellowships- in Neurogenetics at Children's Hospital/Harvard Medical School, and in Neuropharmacology at the Biozentrum in Basel, Switzerland- he joined the faculty of the Human Genetics Department of Yale Medical School. In 1988, he moved to the Boston area to become the Director of the Division of Developmental Neurobiology at the E.K. Shriver Center in Waltham, MA. In 1992, he moved to Case Western Reserve University Medical School and the University Hospitals of Cleveland. While there, he directed the University Alzheimer's Center from 1999 through 2005. In 2006, he moved to the Piscataway/New Brunswick campus of Rutgers University to become Professor and Chair of the Department of Cell Biology and Neuroscience. In July 2012, he moved to Hong Kong to become the Head of Life Sciences at the Hong Kong University of Science and Technology. In 2019, Karl returned to Pittsburgh as a Professor of Neurobiology and an Investigator in the Alzheimer's Disease Research Center at the University of Pittsburgh School of Medicine. He is also Adjunct Professor of Life Science at the Hong Kong University of Science and Technology, where he was formerly Head of Life Sciences. At the same time, he is serving as CTF's Chief Scientific Advisor and hopes to help guide their funded efforts in the fight against dementia.

Abstract:

The field of Alzheimer's disease research focuses heavily on the presence or absence of pathological deposits of the β-amyloid peptide (Aβ). Curiously, much less attention is paid to the normal function of the transmembrane protein from which Aβ is derived. The full-length protein is known as the amyloid precursor protein (APP), even though the Aβ sequence itself makes up only 5-6% of full-length APP. Recently, researchers have turned their attention to the role of full-length APP in modulating neuronal activity. Stimulation of dissociated neuronal cultures with glutamate causes APP message and protein levels to rise 2-3 fold within one hour. The excess protein invades the axon initial segment, which causes it to shorten and move away from the cell body. Both of these changes reduce the probability of action potential firing, quieting the neuron and protecting it from excitotoxicity. These findings have been pursued *in vitro* using high-density multielectrode arrays. The resulting physiological picture of dissociated neuronal cultures has revealed that neurons from APP transgenic mice are altered in their physiological properties from early times in culture, and the networks they establish are clearly different from those of wild type neurons. Altering APP levels in mature cultures causes a different cellular and network response, leading to speculation that familial and sporadic forms of Alzheimer's disease are fundamentally different. This has important implications for the experimental model systems in which new pharmacological therapeutic approaches are tested.

Pathobiology of APOE in Aging and Alzheimer's Disease

Guojun BU

Head and Chair Professor
The Hong Kong University of Science and Technology

Biography:

Prof Guojun BU is the Lo Ka Chung Charitable Foundation Professor of Science, Head and a Chair Professor in the Division of Life Science at the Hong Kong University of Science and Technology. He is a world-renowned neuroscientist and former Chair, Department of Neuroscience at Mayo Clinic. His other career appointments include Professor in Cell Biology and Neuroscience at the Washington University School of Medicine in St. Louis and Chief Scientific Officer at SciNeuro Pharmaceuticals. Prof Bu is a leader in the field of apoE and apoE receptors, which play critical roles in the pathogenesis of Alzheimer's disease (AD). His primary interest is to understand why APOE4 is a strong risk factor for AD and how this pathway can be targeted for therapy. He has published over 380 articles with >48,000 citations and an H-Index of 125 (Google Scholar). He has been named as a "Highly Cited Researcher" by the Web of Science for the past several years. Prof Bu has received numerous honors and awards including the Zenith Fellows Award from the Alzheimer's Association, the Established Investigator Award from the American Heart Association, a MERIT award from NIH, the Investigator of the Year award from the Mayo Clinic, and the MetLife Foundation Award for Medical Research in Alzheimer's disease. He is an elected Fellow of the American Association for the Advancement of Science (AAAS), Founding Editor and Editor-in-Chief of *Molecular Neurodegeneration*, an Associate Editor for *Science Advances*, and is on the editorial board for *Neuron*.

Abstract:

Alzheimer's disease (AD) is the leading cause of dementia in elderly people, impacting an increasingly large population of our aging society. Despite progress in understanding the pathological events associated with AD, the complex molecular events that underlie the development of AD remain poorly understood and are the key to developing targeted therapies. APOE4 allele of the apolipoprotein E (APOE) gene is the strongest genetic risk factor for late-onset AD compared to the common APOE3 allele or the protective APOE2 allele. In the central nervous system (CNS), apoE4 inhibits the clearance and promotes the aggregation of amyloid-β (Aβ) and has several independent effects including age-dependent inferior functions in transporting lipids, supporting synapses, and controlling neuroinflammation. In this presentation, he discusses current understanding of how APOE impacts AD risk with a focus on their own studies using animal models and iPSC-derived cellular and organoid models. Specifically, using human APOE allele-specific and cell type-specific mouse models, they found that apoE isoforms expressed in different cell types in the brain, vasculature, and periphery differentially modulate brain cognition and AD pathology. Highlights will include the effects of peripheral apoE and microglial apoE in brain function and AD pathogenesis in an isoform-dependent manner. Knowledge gained through studies from their group and others can help with designing individualized therapies targeting APOE in a genotype-specific manner.

Novel Mechanisms and Immunotherapy Strategy for Tau Pathogenesis

Yingjun ZHAO

Professor
Xiamen University

Biography:
Prof Zhao is a professor at the School of Medicine, Xiamen University. He received his PhD from Xiamen University and postdoctoral training at the Sanford Burnham Prebys Medical Discovery Institute in San Diego, CA. His research mainly focuses on molecular mechanisms underlying the pathogenesis of tauopathies and development of immunotherapy strategies for treating these devastating diseases. Prof Zhao has published over 40 papers in journals such as *Neuron*, *Molecular Neurodegeneration*, and *Alzheimer's & Dementia*.

Abstract:
The microtubule-associated protein tau is encoded by the MAPT gene. Abnormal accumulation of tau protein in the brain is one of the primary pathological hallmarks for tauopathies such as progressive supranuclear palsy, Pick's disease, and Alzheimer's disease, yet the underlying mechanisms remain to be fully elucidated. Here, they show that both phosphorylation of tau at the 217 site and circular RNA(circTau) derived from the MAPT gene contribute to tau pathogenesis and the associated neurodegeneration. They also show that passive immunotherapy targeting p-tau217 alleviates tau pathology and neurodegeneration in a tauopathic mouse model.

11th Macau Symposium on Biomedical Sciences

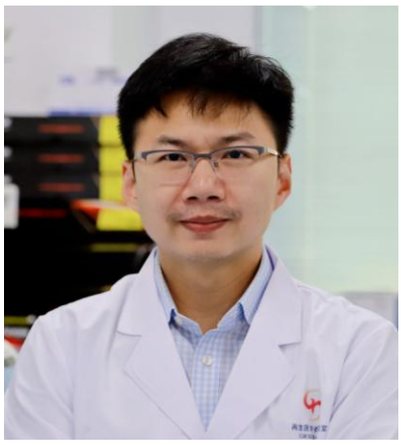
Session III

Session Chair: Guokai CHEN

Session Co-Chair: Ren-He XU

Stem Cell, Gene and Cell Therapy

MIR/SINE-Associated Enhancers Promote TGFβ1-Induced EMT in Lung Cancer Cells



Man ZHANG

Principal Investigator
Guangzhou National Laboratory

Biography:

Prof Man ZHANG is a Principal Investigator at the Basic Research Department of Guangzhou National Laboratory, recipient of the National Overseas High-Level Youth Talent Program, Outstanding Expert of Guangzhou. He graduated with a degree in Biotechnology from Sichuan University in 2007; obtained a PhD in Developmental Biology from the Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences in 2013. He conducted postdoctoral research at the University of Edinburgh from July 2014 to November 2019 with Prof Ian Chambers, and returned to China in December 2019 to set up his own lab. His research work mainly focuses on gene transcriptional regulation and cell fate transition. To date, his work has been published in journals such as *Nature*, *Developmental Cell* and *Cell Reports* etc.

Abstract:

Epithelial-mesenchymal transition (EMT) plays a pivotal role in carcinoma invasion and metastasis; however, the intrinsic enhancers governing this process remain largely uncharacterized. Leveraging genome-wide STARR-seq technology, they systematically identified functional enhancers in TGF-β-induced EMT model, unveiling their regulatory potential in lung adenocarcinoma (LUAD) patients. Further analysis of over 4,000 core mesenchymal enhancers revealed transposon subfamily, within highly active TGFβ1-induced mesenchymal enhancer clusters. Functional depletion of MIR-associated enhancers markedly reduced target gene expression and impaired lung cancer cell migration both *in vitro* and *in vivo*, underscoring their essential role in mesenchymal gene regulation and EMT-driven metastasis. Collectively, this study provides novel insights into the *cis*-regulatory function of MIR elements in the TGFβ1-induced EMT program and highlights potential therapeutic targets for lung cancer treatment.

Xenogeneic Organ Regeneration and Long-Term *In Vitro* Embryo Culture

Jianguo ZHAO

Professor
Institute of Zoology
Chinese Academy of Sciences

Biography:

Prof Zhao, is a distinguished researcher at the State Key Laboratory of Stem Cell and Reproductive Biology, Institute of Zoology, Chinese Academy of Sciences (CAS). Recognized as a National Science Fund for Distinguished Young Scholars recipient and a CAS talent recruit (2010), he leads the Large Animal Genetic Modification Research Group and holds adjunct professional roles at the University of Science and Technology of China and Anhui University. His research focuses on pig functional genomics and genome editing, pioneering methods such as chemical mutagenesis to create genome-wide mutant libraries for identifying genes linked to skeletal development, muscle growth, blood regeneration, and behavior. He has developed groundbreaking models, including transgenic pigs expressing human coagulation factor IX in milk (for hemophilia research) and UCP1-edited pigs with enhanced lean meat yield and thermoregulation, widely covered by global media. Prof Zhao also investigates epigenetic regulation in pig embryogenesis and somatic cell nuclear transfer, aiming to advance biomedical models and livestock breeding. With over 50 SCI publications in journals like *Science Advances*, *PNAS*, and *Blood* (cited 1,000+ times), he serves on editorial boards for *J Mol Cell Biol*, *Fundamental Research*, and others. As Chief Scientist for China's "863" Program and key National R&D projects, he advises on biomedical materials, livestock breeding, and transgenic technology. An active academic contributor, he has delivered 40+ invited talks and holds 6 patents (5 domestic, 1 PCT).

Abstract:

Porcine xenotransplantation offers a promising solution to address the critical shortage of transplantable human organs. While preliminary successes have been achieved in transplanting functional pig-derived hearts, kidneys, and livers into human recipients, persistent immunological rejection remains a major barrier to long-term survival. A transformative approach lies in regenerating human organs within pigs, which could inherently bypass immune rejection. However, low chimeric efficiency of human stem cells in porcine hosts currently limits this strategy. Here, they established a robust *in vitro* culture system for porcine embryos, enabling three germ layers differentiation, gastrulation and providing a platform to assess human stem cell chimerism. Their findings reveal that naive-state human pluripotent stem cells, as well as those treated with a novel "PlanB" protocol, significantly enhance chimeric efficiency within porcine embryos. This breakthrough addresses a key bottleneck in interspecies organogenesis and provides critical insights into optimizing human-porcine cell integration.

Engineering Strategies for Immunocompatible Cell or Organ Allotransplantation

Xiaoqing ZHANG

Distinguished Professor
Tongji University

Biography:

Prof Xiaoqing ZHANG is a Professor in School of Medicine, Tongji University, Shanghai. He obtained his PhD from Fudan University, Shanghai, and then had his postdoctoral training in Waisman Center, University of Wisconsin-Madison. Prof Zhang's research focus is human neural development and cell-based therapy for neurological disorders. With integrated platforms of human embryonic stem cell neural differentiation, genetic engineering, brain organoid culture and human samples, he has uncovered that human neuroectoderm development shows an evolutionarily novel trait, which leads to an "activation-transformation" model for human dorsal-ventral regional patterning. His recent researches have also established sophisticated technologies for non-invasive survey and remote controls of brain allografts, and "off-the shelf" strategies for immunocompatible cell transplantation through genetic engineering in pluripotent stem cells.

Abstract:

Cell and organ transplantation remains the last-resort treatment for most end-stage diseases, yet its efficacy is severely limited by the scarcity of major histocompatibility complex (MHC)-matched donor cells or organs. To address this, they developed a "donor MHC-specific thymus vaccination" (DMTV) strategy, leveraging adeno-associated virus-mediated delivery to stably express allogeneic MHC molecules alongside autologous MHC in the recipient thymus. This approach induces T cell tolerance to both self and donor MHC by eliminating cells reactive to either during thymic education. In C57BL/6 and BALB/c mouse models, DMTV enabled long-term graft tolerance for skin and embryonic stem cell transplants, and its efficacy was further validated in a humanized bone marrow, liver, thymus (BLT) mouse model for human embryonic stem cell transplantation. Parallelly, they also engineered hPSCs with no surface expression of classical human leukocyte antigen (HLA) class I proteins via beta-2 microglobulin (B2M) knockout or biallelic knockin of HLA-G1 within the frame of endogenous solutions to overcome immune rejection, paving the way for universally compatible "off-the-shelf" cell grafts and addressing the critical shortage of MHC-matched donor organs.

11th Macau Symposium on Biomedical Sciences

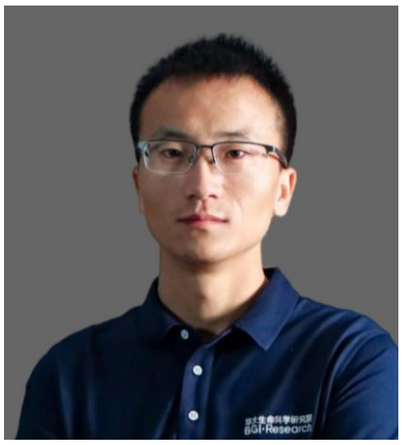
Session IV

Session Chairs:

Tzu-Ming LIU, Xiaofan DING

Frontiers of RNA Sequencing Technology

Spatial Transcriptomic Atlas Reveals Cellular Organization in the Octopus Brain and Implications for Cognitive Capabilities



Guangyi FAN

Chief Scientist
Qingdao Key Laboratory of Marine Genomics
BGI Research

Biography:

Since joining BGI, Dr Fan has been dedicated to research in the fields of comparative genomics and bioinformatics. He has led and initiated research projects such as "Fish10K","M10K+", and "Global Marine Microbial Genomics", promoting the scientific papers have been published in internationally renowned academic journals such as *Nature*, *Science*, and *Cell*. Among them, more than 40 papers were published as the first author or corresponding author (including co-authors), with a cumulative citation count of more than 16,000 times and an h-index of 52. Among them, the research results on Antarctic krill genomics were selected as one of the "Top 10 Marine Science and Technology Advances in China in 2023" and the "First Prize of Natural Science Award of Qingdao City". The construction of the Marine microbiome database was selected as one of the "Top Ten Scientific and Technological Innovation Achievements of Shandong Province" and one of the "Top Ten Scientific and Technological Advances in China's Ocean and Limnology in 2024". He has led or participated in over ten national, provincial and municipal projects, including a National Natural Science Foundation of China general project, a sub-project of the National Key Research and Development Program, and an outstanding youth project of the Guangdong Provincial Basic and Applied Basic Research Foundation Committee.

Abstract:

Octopuses have evolved impressive neural systems and sophisticated cognitive capabilities. However, the specific spatial cellular organization in the octopus brain, as well as the differences between octopuses and humans, remain largely elusive. Here, they utilized a combination of spatial transcriptomics sequencing (stereo-seq), snRNA-seq, and scRNA-seq techniques to establish a cell transcriptomic atlas of the octopus brain. This atlas, composed of 33 cell types, reveals distinct spatial patterns of cells in octopus brain potentially linked to the functionality of specific anatomical regions. By leveraging the stereo-seq data, they categorized 26 neuronal subtypes based on their discernible distribution patterns, enabling accurate assessment of cellular heterogeneity. Notably, they found that dopaminergic neurons N-ACHO-8 play a vital role in the memory circuit of the vertical lobe, indicating a homology between the cellular mechanism underlying short- and long-term memory in octopuses and the cortex and hippocampus of mammals. They also identified a unique cell population, Myoc+ astrocytes, prominently enriched in the outer granular layer of the optic lobe in octopuses, demonstrating that octopuses have evolved an anatomical domain that closely resembles the glia limitans superficialis of mammals. These shared genetic programs suggest a conservation of fundamental memory processes mechanisms across species.

AI-Driven mRNA Therapeutics: Algorithms and Applications

Liang ZHANG

Professor
Hangzhou Institute of Medicine
Chinese Academy of Sciences

Biography:
Prof Zhang is a Researcher and PhD advisor at the Hangzhou Institute of Medicine, Chinese Academy of Sciences. He holds a PhD in Computer Science and previously worked at Baidu in Silicon Valley, where he focused on AI-driven drug development. His current work centers on nucleic acid-based therapeutics, including mRNA and RNAi drug design and personalized cancer vaccines. He developed the LinearDesign algorithm, published in *Nature* in 2023, and later introduced circDesign, which improves the circularization efficiency and expression of circular mRNA. He contributed to the design of an mRNA COVID-19 vaccine that received emergency use approval in Laos, and several of his mRNA vaccines targeting cancer and infectious diseases are currently in clinical development.

Abstract:
This talk introduces recent work on the algorithmic design of mRNA therapeutics. It focuses on AI-based approaches developed to improve sequence stability and expression, with examples of their applications in vaccine development and related areas.

Stereo-Seq, A High-Resolution and Large-Field Spatial Multi-Omics Technology

Ying HE

Technical Expert
BGI-Shenzhen

Biography:
Dr Ying HE is a Technical Expert in Spatial Transcriptomics at BGI Research. Dr HE obtained his PhD in Developmental Biology from the College of Life Sciences, Zhejiang University in 2013. Following his doctorate, Dr He conducted genomics research at the South China Sea Institute of Oceanology, Chinese Academy of Sciences (CAS), and subsequently pursued biophotonics research at Shenzhen University. Dr He has authored multiple research articles published in leading international journals, including *Chem*, *Nature Communications*, *Chemical Communications*, and *Developmental Biology* etc. Dr He is also an inventor on six pending patents. Dr He spearheaded the development of Spatial Transcriptomics techniques for FFPE samples. Dr He is currently leading further R&D efforts to advance novel Spatial Transcriptomics technologies.

Abstract:
Stereo-seq is a spatial omics technology developed on high-throughput sequencing chips, which is distinguished by its ultra-high resolution and large field of view. It enables multi-omics analyses, including spatial transcriptomics and proteomics, on both fresh-frozen and formalin-fixed paraffin-embedded tissues, and is capable of spatial single-cell analysis.

Leveraging Single-Cell RNA-Seq and Organoid Technology for Establishing a Biosynthetic Food Safety Assessment System

Jian HE

Associate Professor
Shanghai Jiao Tong University

Biography:
Prof He is the Director of Single Cell Sequencing Core, focuses on the development and application of single-cell multi-omics analysis technology, especially the use of new single-cell technologies and strategies to explore the pathogenesis of tumours and other major diseases at the single-cell level and the evolution of the tumour microenvironment under the intervention of drugs or the external environment, to discover new targets for tumour prevention and control and to carry out drug screening and repositioning on the basis of this, to explore new strategies for the diagnosis and treatment of tumours and clinical translation; he also created a system of biosynthetic food, drug, and environmental pollutant risk assessment based on single-cell sequencing, organoid, and other models for application in food, nutrition, and health.

Abstract:
Single-cell transcriptome sequencing is a powerful tool for revealing cellular heterogeneity, differentiation and developmental relationships between cells, and intercellular communication, while organoids, which can mimic real organs in structure and function, have become an optimal tool for studying disease progression, anticancer drug screening, drug toxicity assays, and gene and cell therapies, both of which have been recognized as technologies of the year by *Nature Methods*. Now, the combination of the two can better analyze the degree of similarity between organoids and real organs at the cellular, genetic and molecular levels, monitor the dynamic transcription in organoids, and study the interactions and signaling between organoid cells, which is bound to become an important tool in the field of cutting-edge medical research. Recently, they have established an *in vitro* evaluation system for a variety of nutrients and functional foods by combining single-cell transcriptome sequencing and organoid technology, and applied it to the evaluation of functional components of breastmilk, which provides a new way of analyzing the effects of nutrients on the human body and developing infant formulae more suitable for Chinese babies.

11th Macau Symposium on Biomedical Sciences

Session V

Session Chairs:

Qi ZHAO, Zhenghai TANG

Tumour Immunology and Immunotherapy

Phase-Separated Molecular Coacervates for Intracellular Delivery and Immunotherapies

Jiang XIA

Professor
The Chinese University of Hong Kong

Biography:
Prof Xia is a professor in the Department of Chemistry and a professor by courtesy in the School of Life Sciences at the Chinese University of Hong Kong (CUHK). He received a Bachelor of Science (1995-1999) and a Master of Science degree (1999-2002) from Nanjing University, China, and a PhD degree from Stanford University, USA (2002-2006). He received postdoctoral training at Caltech and concomitantly held the associate position at the Howard Hughes Medical Institute, USA, from 2007 to 2008. He started his independent career as an Assistant Professor (2009-2014), was promoted to tenured Associate Professor (2015-2021), and is now a Professor at CUHK. His research interests lie at the interface of chemical biology, synthetic biology, and biomaterials, focusing on the application of chemistry in biomedicine (Chem4BioMed) and in synthetic biology (Chem4SynBio). His lab currently focuses on the following projects: 1. Site-specific antibody reactions and their applications in immunotherapy; 2. Phase separation and molecular coacervation for biosynthesis and intracellular delivery; 3. Exosome-targeted drug delivery in osteoarthritis and other diseases; 4. Recombinant collagen for tissue regeneration. He was elected a Fellow of the Royal Society of Chemistry in 2021. He is a co-founder, chief scientist, or chief consultant of several companies.

Abstract:
Delivering biotherapeutics across the cell membrane is a challenging task. They discovered that molecules forming phase-separated coacervates can convey biological molecules, such as siRNA, mRNA, peptides, and proteins, including antibodies, into the cytoplasm of cells. These technologies have ignited new cancer therapies, including targeted protein degradation, immune cancer therapies, and mRNA vaccines, among others.

Targeting Airway Epithelial Cells to Translate Mechanism into Therapy

Roger Mingtao LIANG

Associate Professor
University of Newcastle

Biography:

Prof Roger Mingtao LIANG is an investigator in Hunter Medical Research Institute and pharmacy research leader in the School of Biomedical Science and Pharmacy at the University of Newcastle. His research group works on mechanistic understanding of nanoparticle interaction with biological systems, with a specific focus on improving cell-specific uptake and sub-cellular localization of therapeutic nanoparticles. It combines basic research/mechanistic studies with a strong translational interest through their multidisciplinary collaborations to develop transformative nanomedicines for reproduction, cancer and respiratory diseases.

Abstract:

Airway epithelium is the first line of defence against respiratory virus infections. It is now recognised that airway epithelium plays a central role in immunity and is involved in the development of respiratory diseases like asthma and chronic obstructive pulmonary disease (COPD). In his talk, Prof Liang discusses targeted delivery of TLR agonists and mitochondrial feasibility of modulating their immune response to prevent and treat respiratory virus infections.

Macrophage and Tumour Immunotherapy

Jun CHEN

Professor
Sun Yat-sen University

Biography:

Prof Jun CHEN, a professor at the School of Medicine, Sun Yat-sen University, obtained a bachelor's degree from Wuhan University in 2007 and a doctorate degree from the Institute of Biophysics, Chinese Academy of Sciences in 2013. From 2013 to 2018, he did postdoctoral research at the Montreal Clinical Research Institute in Canada. In 2018, he joined Sun Yat-sen University. He mainly focuses on the research of the regulatory mechanisms of the tumour immune microenvironment, as well as the exploration of new targets and novel therapies for tumour immunotherapy. Several new targets have been in the process of being transformed into First in Class innovative drugs. At present, he has published a number of research articles in top journals such as *Nature* (2017), *Nature Cancer* (2023, 2024, both are "ESI Highly Cited Papers"), *Science Immunology* (2025), and *Science Advances* (2025). He has reported multiple new targets of macrophages and put forward a new concept of "targeting macrophages to reprogram the tumour immune microenvironment (ReTime)".

Abstract:

Prof Jun CHEN has carried out a series of systematic work focusing on tumour-associated macrophages (TAMs). They have revealed the important immune receptors and immune signaling pathways on macrophages, discovered the key subsets and characteristic markers of macrophages in the tumour microenvironment, and deciphered the key molecular signaling mechanisms that regulate the spatial distribution, fate decision-making, antigen presentation, and functional plasticity of macrophages. This has provided an in-depth understanding of the functional mechanisms of macrophages and also laid a solid theoretical foundation and provided a series of novel targets for macrophage-based tumour immunotherapies.

Regulation of Lipid Metabolism in Tumour-Infiltrating CD8+ T Cells

Jun GUI

Professor
Shanghai Jiao Tong University

Biography:

Prof Gui obtained her PhD degree in Immunology from Shanghai Medical College, Fudan University at Shanghai, China. She received her postdoctoral training in tumour immunology at University of Pennsylvania from 2014-2020. Currently she is a Principal Investigator at Renji-Med X Clinical Stem Cell Research Center, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University. Her research focuses on the immune regulation of tumour microenvironment (TME). Specially, her lab is interested in deciphering the mechanisms underlying CD8+ T cell dysfunction in TME and the generation of pre-metastatic niche. She has published multiple papers in the high impact journals including *Cell Metabolism* (2024), *Nature Cancer* (2020), *Cancer Cell* (2019, 2017), *Advanced Science* (2024), *Cancer Immunology Research* (2025). She was awarded as Shanghai Overseas Talent (2021) and National Excellent Young Investigator (2024).

Abstract:

Lipid accumulation is considered one of the key characteristics of most solid tumours. Lipid metabolism not only affects tumour cells themselves but also plays a crucial role in other cells within the tumour microenvironment (TME), particularly immune cells. CD8+ T cells are key effector immune cells responsible for killing tumour cells. However, they often exhibit functional exhaustion within TME. They identified that tumour cells abnormally secreted the endocrine factor FGF21. Numerous studies demonstrate that FGF21 plays a vital role in maintaining metabolic homeostasis and has therapeutic potential in metabolic disorders such as obesity and type II diabetes. However, tumour-secreted FGF21 binds to the FGFR1-KLB receptor complex on activated CD8+ T cells, leading to persistent activation of the AKT-mTORC1-SREBP1 signaling pathway. This results in excessive cholesterol synthesis, thereby inducing functional exhaustion of tumour-infiltrating CD8+ T cells. FGF21 blockade using a neutralizing antibody normalized AKT-mTORC1 signaling and reduced excessive cholesterol accumulation in CD8+ T cells, thus restoring CD8+ T cell cytotoxic function and improving the efficacy of anti-PD-1 immunotherapy. Furthermore, they revealed that the lipolysis of cancer-associated adipocytes (CAAs) is a key factor contributing to lipid accumulation in the TME. Adipocyte-derived FGF21 acts in an autocrine manner to activate FGFR1/KLB/p38 pathway, inducing upregulation of adipose triglyceride lipase (ATGL). This process drives CAA lipolysis, releasing free fatty acids, which subsequently cause lipid peroxidation in CD8+ T cells, disrupt mitochondrial homeostasis, and ultimately lead to CD8+ T cell exhaustion. In summary, they have identified FGF21 as a key regulator of lipid metabolism in tumour-infiltrating CD8+ T cells, driving their functional exhaustion, suggesting that inhibiting FGF21 could be a valuable strategy to enhance the cancer immunotherapy efficacy.

Functions of Microglia in Alzheimer's Disease

Shoutang WANG

Assistant Professor
The University of Hong Kong

Biography:

Prof WANG completed his PhD work at Institute Gustave-Roussy, France, where he was trained in the developmental hematopoiesis of myeloid lineage. After receiving his PhD degree in 2017, he joined in Prof Marco Colonna's lab at Washington University School of Medicine in the St. Louis, USA. In Colonna lab, he contributed to multiple projects that aided him in investigating the role of the function of TREM2 in microglia in the mouse model of Alzheimer's disease. Following his postdoctoral training, he joined School of Biomedical Sciences, the University of Hong Kong, to establish his own laboratory in 2023. He received the NSFC Excellent Young Scientists Fund in 2024. His lab is particularly interested in learning how the immune system interacts with the central nervous system during neurodegenerative diseases.

Abstract:

Genetic studies have highlighted microglia as pivotal in orchestrating Alzheimer's disease. Microglia that adhere to Aβ plaques acquire a transcriptional signature, "disease-associated microglia", which largely emanates from TREM2-DAP12 receptor complex that transmits intracellular signals through the protein tyrosine kinase SYK. The human TREM2 R47H variant associated with high Alzheimer's disease risk fails to activate microglia via SYK. They found that SYK-deficient microglia cannot encase Aβ plaques, accelerating brain pathology and behavioral deficits. SYK deficiency impaired the PI3K-AKT-GSK-3β-mTOR pathway, incapacitating anabolic support required for attaining the disease-associated microglia profile. However, SYK deficient microglia proliferated and advanced to an Apoe-expressing prodromal stage of disease-associated microglia; this pathway relied on the adapter DAP10, which also binds TREM2. Thus, microglial responses to Aβ involve non-redundant SYK- and DAP10-pathways. Systemic administration of an antibody against CLEC7A, a receptor that directly activates SYK, rescued microglia activation in mice expressing the TREM2 R47H allele, unveiling new options for Alzheimer's disease immunotherapy.

11th Macau Symposium on Biomedical Sciences

Session VI

Session Chairs:

Yunlu DAI, Bei LI

Biomaterials and Nanomedicine

Microneedle Technology for Intradermal Cell Delivery

Chenjie XU

Professor, Associate Dean
City University of Hong Kong

Biography:

Prof Xu Chenjie graduated from Nanjing University in 2002, obtained a master's degree from the Hong Kong University of Science and Technology in 2004, and obtained a doctorate from Brown University in 2009. He has conducted research at Stanford University (visiting scholar), Harvard Medical School (research associate) and Nanyang Technological University (assistant professor). He develops novel drug delivery formulations and devices. He is well known for the inventions of self-illuminating quantum dots, Framework nucleic acids for transdermal drug delivery, microneedle device for intradermal cell delivery and anesthetics delivery in dentistry. He also develops skin patch for extracting skin interstitial fluid to monitor the health conditions. He is a recipient of "National Science Fund for Distinguished Young Scholars" from National Natural Science Foundation of China and has been ranked as "Top 2% most highly cited scientists" by Stanford University since 2021.

Abstract:

The advancement of cell therapy in treatment of skin disorders created a need for simple, safe and efficient transdermal delivery of therapeutic cells. Here he presents their microneedle (cryoMN) platform which functions as payload vehicle of living cells, achieving transdermal delivery of cells in a minimally invasive manner. CryoMNs is fabricated by stepwise cryogenic micromolding of the optimized cryogenic medium and pre-suspended desired cells in the pre-designed MN mold. CryoMNs show comparable mechanical strength to existing MN platforms and can be easily inserted into the skin. *In vitro* and *in vivo* results reveal that the loaded cells can retain viability and proliferative capability after being deployed from cryoMNs. One potential application of cryoMNs is demonstrated through intradermal delivery of ovalbumin-pulsed dendritic cells (OVA-DCs) for DC-based cancer immunotherapy. Vaccination with OVA-DCs loaded cryoMNs elicits robust antigen-specific immune responses and provides potent prophylactic protection against tumour in mice, which are superior to the therapeutic outcomes by conventional standard vaccination methods such as subcutaneous and intravenous injection of OVA-DCs. Finally, they also found that this device can be used to deliver other types of cells like T cells, melanocytes, and bacteria.

Oxyberberine Nanoparticle as a Novel Agent for Alzheimer's Disease: Evaluation of Its Efficacy and Molecular Mechanisms

Yanfang XIAN

Assistant Professor
The Chinese University of Hong Kong

Biography:

Prof Yanfang XIAN is the Assistant Professor and Programme Director of Master of Science in Chinese Medicine at School of Chinese Medicine, The Chinese University of Hong Kong. Prof Xian obtained her PhD degree in 2013 from The Chinese University of Hong Kong. Her research interests are the pharmacology of Chinese medicine in Alzheimer's disease, pancreatic cancer, prostate cancer. So far, Prof Xian has published more than 100 original research articles based on her experimental findings in various SCI-listed academic journals such as *Molecular Cancer*, *Acta Pharmaceutica Sinica B*, *Journal of Experimental & Clinical Cancer Research*, *Journal of Advanced Research*, *Journal of Neuroinflammation*, *Brain, Behavior and Immunity* with the H-index of 42 of Google Scholar. Over the past 5 years, Prof Xian had successfully obtained more than ten external competitive grants. In addition, Prof Xian is listed as World's Top 2% Scientists by Stanford University.

Abstract:

Alzheimer's disease (AD) is one of the most prevalent neurodegenerative diseases characterized by progressive cognitive dysfunction and behavioural impairments. No effective treatment is currently available to slow down or stop the progress of AD. Oxyberberine (OBB), one of the main metabolites of berberine derived from intestinal and erythrocyte metabolism, exhibits similar effects to berberine which has neuroprotective effects in various central nervous system (CNS) diseases including AD. OBB-hydroxypropyl-β-cyclodextrin (OBB-β-CD) was prepared to increase the water solubility and improve plasma concentration-effect relationship of OBB. The results indicated that OBB-β-CD was more potent than free OBB in improving cognitive impairments in 3×Tg mice via inhibiting Aβ deposition, tau hyperphosphorylation and neuroinflammation through suppressing the activation of CXCR3 and microglial. OBB-β-CD also more potently modulated the gut microbiota community to protect its stability than free OBB. These results suggest that OBB-β-CD has good potential for further development into therapeutic agent for AD treatment.

Smart Nanomedicines Acting on Tumour Vessel Microenvironment

Suping LI

Professor
National Center for Nanoscience and Technology
University of Chinese Academy of Sciences

Biography:

Prof Suping LI is a Full Professor at the National Center for Nanoscience and Technology of China (NCNST) and at the University of the Chinese Academy of Sciences (UCAS). Her research interests are in nanomedicines and the design of biology-inspired nanomachines to address the currently known barriers in tumour vessel-targeted therapy and targeted thrombolysis therapy. In recent years, she has published several papers in prestigious journals such as *Nature Biotechnology*, *Nature Materials*, *Nature Biomedical Engineering*, *Nature Reviews Cancer*, and among others, as the co-first/corresponding author. Her work has been extensively acknowledged by her international peers, and highlighted by prestigious journals (e.g., *Nature Reviews Drug Delivery*, *Nature Reviews Cancer*). One of her studies was selected as a Chinese 'Technical Advances Top Ten' and 'Top Technical Advances' in the world in 2018. Prof Li holds seven patents (three of the Chinese patents are under consideration for clinical use) and she has been invited to present at numerous biomaterials- and biotechnology-related international conferences, such as the 14th Asian Congress in Biotechnology (ACB 2019), and the 4th International Conference on Nanomedicine (ChinaNanomedicine 2021). Her interests are majorly in two directions: (1) Design of biology-inspired nanomachines/nanodrugs to address the currently known barriers in tumour vessel targeted therapy; (2) Preclinical translation of antitumour or thrombolysis nanodrugs.

Abstract:

Like normal organs, tumours need to establish a blood supply to satisfy their demand for oxygen and nutrients and accomplish metabolic functions. However, tumour vessels display considerable variation in the patterning and properties, as well in their responses to vessel targeted therapy. Based on the potential vulnerabilities that could be targeted in vascular system, they developed several nanorobotic drugs to selectively infarct tumour vessels or modulate microenvironmental components to achieve safe and effective antitumour therapy. For achieving targeted tumour vessel occlusion, they have designed an autonomous, tubular DNA nanorobots capable of specifically binding to the tumour vascular endothelium and presenting the coagulation protease thrombin to locally induce tumour infarction and necrosis. They also developed the intelligent and peptide nanodrugs that deplete intratumoural platelets, dramatically enhancing the permeability of tumour vessels and thus stimulating the accumulation of chemotherapeutic drugs within tumour tissues. With this seminal work in the development of nanorobot based anticancer therapeutics, it may be asserted that 'swallowing the doctor' may not be too far away.

11th Macau Symposium on Biomedical Sciences

Session VII

Session Chair: Chris WONG

Session Co-Chair: Marta Filipa SIMÕES

Fungi in One Health

Host-Induced Fungicide Phenotypic Resistance

Linqi WANG

Deputy Director and Professor
Institute of Microbiology
Chinese Academy of Sciences

Biography:

Prof Linqi WANG, Deputy Director of the Institute of Microbiology, Chinese Academy of Sciences (CAS), is a recipient of the National Science Fund for Distinguished Young Scholars and CAS "Hundred Talents Program“ (rated"Excellent"). His research focuses on human pathogenic fungi and antifungal strategies. He pioneered fungal phenotypic resistance studies, co-discovered the multidrug-resistant novel pathogen *Rhodosporidiobolus fluvialis*, and developed improved treatments for fungal meningitis. Using drug repurposing, he identified FDA-approved drugs targeting fungal persisters and a high-resistance-barrier antifungal. He has published in *Nature Microbiology* (3x), *Cell Host & Microbe*, and *Nature Communications* as corresponding author. He chairs the Microbial Genetics Committee of the Chinese Society of Genetics and advises the National Fungal Disease Surveillance Network.

Abstract:

Human pathogenic fungi pose a serious threat to human health and safety. Unfortunately, the limited number of antifungal options is exacerbated by the continuous emergence of drug-resistant variants. Recent studies have also highlighted the importance of other modes of fungal survival of antifungal treatment, including fungistatic tolerance and fungicidal phenotypic resistance(fungicide tolerance and persistence) indicating the complexity of the fungal response to antifungal drugs. However, whether fungicide tolerance or persistence can be induced by host-derived factors during fungal diseases remains largely unknown. Through a systematic evaluation of metabolite-drug-fungal interactions in the leading fungal meningitis pathogen, *Cryptococcus neoformans*, they found that brain glucose induces fungal tolerance to amphotericin B (AmB) in mouse brain tissue and patient cerebrospinal fluid via the fungal glucose repression activator Mig1. Mig1-mediated tolerance limits treatment efficacy for cryptococcal meningitis in mice via inhibiting the synthesis of ergosterol, the target of AmB, and promoting the production of inositolphosphorylceramide, which competes with AmB for ergosterol. They also demonstrated that highly AmB-tolerant fungal persister cells can form during cryptococcal lung infections and identified the FDA drug with potent activity against fungal persister cells through a drug repurposing approach. His group is now investigating the genetic basis that differentiates antifungal resistance, tolerance and persistence.

Insight into Fungal Pathogenicity Driven by Regulation of Secondary Metabolism

Wenbing YIN

Professor
Institute of Microbiology
Chinese Academy of Sciences

Biography:

Prof Wen-Bing YIN received his PhD (2009) from the University of Marburg in Germany, under the direction of Prof Shu-Ming Li. Then he worked with Profs Nancy Keller and Yi Tang as a postdoctoral fellow at the University of Wisconsin-Madison (2009-2012) and at the University of California in Los Angeles (2012-2013), respectively. In 2014, he joined the Institute of Microbiology, Chinese Academy of Sciences, as a principal investigator. He also acts as a Professor of University of Chinese Academy of Sciences, adjunct Professor of University of Science and Technology of China. His research group is engaged in the synthetic biology of fungal natural products, including the activation of fungal silencing gene clusters, the construction of universal fungal expression system and the creation of synthetic biology of drug active compounds. He has published more than 120 papers in *Sci. Adv.*, *Nat. Commun.*, *Nat. Chem. Biol.*, *J. Am. Chem. Soc.*, *Angew Chem* and other international journals. He is the executive director of the Chinese Society of Mycology and the chairman of the Professional Committee of Medicinal fungi of the Chinese Society of Mycology. Prof Yin is the associate editor of the international journals *Fungal Genetics and Biology*, *Mycology* and *Frontiers in Fungal Biology*.

Abstract:

Fungal pathogens threaten human health and ecosystems, with their virulence often orchestrated by secondary metabolites (SMs). Here, they uncover a regulatory hub in *Aspergillus fumigatus* that coordinates pathogenicity through a specialised metabolite network. Using a multi-omics combined chemistry strategy, they identified FqC as a keystone metabolite enabling SM synthesis—as a linchpin controlling metabolic virulence. Central to this process is the RNA-binding protein CsdA, which forms a dynamic nuclear complex with the global regulator LaeB, bridging metabolic remodeling to infection mechanisms. Disruption of the CsdA-LaeB complex hyperactivated secondary metabolism, amplifying fungal colonisation and pathogenicity. Deconstructing this hub revealed PptA—a phosphopantetheinyl transferase essential for SM biosynthesis. Strikingly, FDA-approved drugs targeting PptA suppressed FqC biosynthesis, reduced fungal burden, and attenuated lung inflammation in murine infection models. These findings highlight how fungal pathogens exploit regulatory nodes, such as the CsdA-LaeB-FqC axis, to synchronise SM production with host invasion. By integrating multi-omics tools and chemical biology, this work advances mechanistic insights into SM-driven pathogenicity and identifies druggable targets (e.g., PptA) for antifungal therapies. Targeting such hubs offers a promising strategy to disrupt fungal virulence networks and combat drug-resistant infections in clinical and agricultural settings.

Mandimycin: A New Polyene Macrolide Antifungal with a Unique Mode of Action

Zhuo SHANG

Professor
Shandong University

Biography:
Prof Zhuo SHANG is a Professor in the School of Pharmaceutical Sciences at Shandong University, China. He earned his PhD in Marine Natural Product Chemistry in 2016 from The University of Queensland supervised by Prof Rob Capon. During 2016-2020, he conducted postdoctoral research at the Scripps Institution of Oceanography, UCSD (with Prof Bill Fenical) and The Rockefeller University (with Prof Sean Brady), focusing on antibiotic discovery from marine and uncultivable bacteria using antibiotic (meta)genomics and metabolomics approaches. In 2020, he returned to Australia as a Research Associate at the University of Western Australia (with Prof Yit-Heng Chooi), working on fungal natural product biosynthesis. Since 2022, he has led an independent research group at Shandong University in China, with the interests in antibiotic discovery, biosynthesis and antimicrobial mechanism of action using integrated approaches that combine genomics, molecular biology, chemical biology and natural product chemistry. To date, Prof Shang has published 50 research articles in peer-reviewed journals, including *Nature*, *JACS*, and *Angewandte Chemie*, with an h-index of 21.

Abstract:
The increasing prevalence of multidrug-resistant fungal pathogens poses a significant challenge to medical treatment, highlighting the urgent need for antifungal antibiotics with novel mechanisms of action. Here, they report the discovery of mandimycin, a glycosylated polyene macrolide antifungal, from *Streptomyces netropsis* using a phylogeny-guided natural product discovery platform. Unlike reported polyene macrolides (e.g., amphotericin B) that target ergosterol in fungal cell membrane, mandimycin binds various types of phospholipids in fungal cell membrane, ultimately leading to cell death. This unique mechanism of action is attributed to its deoxy sugar moiety. Mandimycin exhibits potent and broad-spectrum fungicidal activity, effectively eliminating multidrug-resistant fungal pathogens, including amphotericin-resistant Candida auris, in both *in vitro* and *in vivo* mouse infection models. Moreover, it demonstrates higher aqueous solubility and lower renal toxicity than amphotericin B, making it a promising candidate for antifungal drug development.

Fungi and Cancer: From Gut to Intratumour

Ningning LIU

Professor
Shanghai Jiao Tong University School of Medicine

Biography:
Prof Liu obtained his PhD from Shanghai Institutes of Biological Sciences, Chinese Academy of Sciences in 2012. After graduation, he continued his research in Harvard Medical School/Boston Children's Hospital as a post-doctoral researcher. In 2017, he joined Shanghai Jiao Tong University School of Medicine as a faculty member until now. Prof Liu's research has been focused on fungal infection and cancer progression, especially the mechanistic investigation of fungi-host interaction. He has published more than 70 original papers in prestigious journals (*Cancer Cell*, *Cell Host & Microbe*, *Nature Microbiology*, *Nature Communications*, *Nature Protocols*, *PNAS, Cell Research*, *Cell Reports*, *PLOS Pathogens*, *PLOS Genetics*, etc) and has been licensed 4 patents for invention.

Abstract:
Polymorphic microbiomes have been defined as the emerging hallmark of cancer. In addition, the infectious pathogens are strong and modifiable causes of cancer. When cancer prevention is largely considered in a non-communicable disease context, there is a crucial need for resources directed particularly in high-risk populations. Such interventions can markedly reduce the increasing cancer burden and associated mortality. Yet far less is known about the biological functions of fungi in human cancer. They have been focusing on the causal relationship between fungal infection and cancer progression, mainly from three perspectives including mycobiome, fungi-host interaction and host immune response. This talk will cover all the recent work in their lab. These findings suggest that the mycobiome, albeit at low biomass from gut to intratumour, could be targeted at the strain level to improve the outcome of cancer patients.

A Gut Fungal Symbiont Activates Intestinal Regeneration

Chen DING

Professor
Northeastern University

Biography:
Prof Ding is a Professor and investigator specialising in pathogenic yeast infections. His research employs Cryptococcus spp.—fungal pathogens causing pneumonia and meningitis—to dissect copper ion homeostasis, protein post-translational modifications, and folding mechanisms driving fungal virulence, using murine infection models to identify therapeutic targets. His work has been published in top-tier journals, including *Cell Host & Microbe*, *Nature Chemical Biology*, and *Nature Communications*. Prof Ding was selected as a "Leading Talent" in Shenyang's High-Level Talent Program and honoured by Liaoning Province's Xingliao Plan (Youth Top Talent) and the "Young Talents Project." He mentors award-winning teams in the International Genetically Engineered Machine (iGEM) competition, securing three gold and one silver medals. His academic distinctions include the China Scholarship Council's National Outstanding Self-Funded International Student Scholarship and Duke University's "Duke Scholar in Infectious Disease" title.

Abstract:
The intricate mechanisms governing intestinal repair remain only partially characterised, with emerging evidence suggesting underappreciated roles for commensal microorganisms in mucosal regeneration. While bacterial contributions to gut homeostasis have been extensively studied, the functional impact of fungal species—a critical yet overlooked component of the gut mycobiome—on epithelial healing remains undefined. Here, they identify a commensal fungus as a potent driver of intestinal stem cell (ISC) differentiation and tissue repair. Through comparative analyses with non-functional fungal controls, they demonstrate that Gf uniquely stimulates crypt-like maturation in intestinal organoids. In murine models of dextran sodium sulphate-induced colitis and 5-fluorouracil-mediated intestinal injury, Gf administration accelerated mucosal restitution, restoring epithelial barrier integrity and resolving inflammation. This work establishes the first causal link between a defined fungal species and ISC-mediated regeneration, challenging the conventional bacterio-centric view of gut repair. By demonstrating Gf's capacity to bridge microbial ecology with tissue healing, they redefine the mycobiome as a rich source of therapeutic biologics. Their findings provide a prototype for precision mycobiome interventions, offering a translatable approach to enhance mucosal recovery in inflammatory bowel diseases, chemotherapy-induced mucositis, and other disorders marked by impaired epithelial regeneration. This paradigm shift underscores the clinical potential of harnessing fungal commensals as next-generation regenerative therapeutics.

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