7th

Celebrating the 40th Anniversary of the University of Macau:

Macau Symposium on Biomedical Sciences

23-24 July 2021

澳門大學 UNIVERSIDADE DE MACAU UNIVERSITY OF MACAU

健康科學學院 Faculdade de Ciências da Saúde Faculty of Health Sciences

Programme Booklet

Faculty of Health Sciences, University of Macau

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Welcome to the 7th Macau Symposium on Biomedical Sciences 2021

The Faculty of Health Sciences of the University of Macau (UM) is delighted to welcome you to our annual event highlighted: 7th Macau Symposium on Biomedical Sciences 2021. This year, the symposium is going to be held on 23 and 24 July 2021 at University Hall (N2). In response to the epidemic, this year's symposium will be held in a format that combines online (via ZOOM) and in-person elements, in order to allow participants from around the world to participate in the event. Participants who are unable to attend the symposium in person can join the meeting on ZOOM.

The field of biomedical research is an exciting and ever-expanding area to explore. Our annual Macau Symposium on Biomedical Sciences aims to continue to gather talented and inspired scholars and professionals to foster discussions, knowledge sharing and potential collaborations. This year, the theme of the symposium is DISCOVERY, which includes but not limited to the following topics:

1. Autophagy in Health and Disease
2. Cancer Etiology and Treatment
3. Genome Organization in Development and Disease
4. Neuroscience, Aging and Degenerative Diseases
5. Recent Advance in Drug Discovery and Delivery
6. Stem Cells, Development and Aging
7. Traditional Medicines and Drug Discovery
8. Tumor Immunology and Immunotherapy

In 2019, we were grateful to have gathered over 400 participants and scholars from ten different regions. Particularly, it was our pleasure to have Aaron Ciechanover, Nobel Laureate in Chemistry 2004 and George Fu GAO, Director of Chinese Center for Disease Control and Prevention, National Natural Science Foundation of China presented at the symposium.

This year, we are very honoured that Lieping CHEN, United Technologies Corporation Professor in Cancer Research and Professor of Immunobiology, of Dermatology and of Medicine (Medical Oncology); Co-Leader, Cancer Immunology, Yale Cancer Center is going to be our keynote speaker. In addition, renowned scientists, including Shaorong GAO, Professor and Dean of the School of Life Sciences and Technology, Tongji University; John Mekalanos, Adele H. Lehman Professor of Microbiology and Molecular Genetics, Harvard Medical School; Noboru MIZUSHIMA, Professor of Graduate School and Faculty of Medicine, The University of Tokyo; and Mingjie ZHANG, Dean of School of Life Sciences, Southern University Of Science And Technology will also be sharing their latest research in this symposium.

On behalf of the organizing committee, I welcome your participation in this exciting event. I sincerely look forward to seeing you at UM in July 2021.

Conference Chair

Chuxia DENG

Dean and Chair Professor, Faculty of Health Sciences
University of Macau

Day ONE: 23 July 2021 (Friday) – AM
Venue: N2 - University Hall

08:30	註冊 Registration 嘉賓接待 Guest Reception
	第七屆澳門生物醫學科學研討會開幕禮 **Opening Ceremony of the 7th Macau Symposium on Biomedical Sciences**
09:00	澳門大學校長宋永華教授致歡迎辭 Welcome Remarks delivered by Prof. Yonghua SONG Rector of the University of Macau 澳門大學健康科學學院院長鄧初夏教授進行大會簡介 Programme Introduction delivered by Prof. Chuxia DENG Dean of the Faculty of Health Sciences of the University of Macau 大合照 Group Photo
	Online Plenary Session - Cutting Edge Science and Translational Medicine **Session Chair: Prof. Chuxia DENG & Prof. Hanming SHEN**
09:15	**Keynote: Prof. Lieping CHEN** **Yale University, USA** *Immunotherapy: A New Era for Cancer Treatment*
09:50	**Prof. John MEKALANOS** **Harvard Medical School, USA** *Protein Covariance Networks Reveal Interactions Important to the Emergence of Viral and Bacterial Pathogens*
10:20	**Prof. Noboru MIZUSHIMA** **The University of Tokyo, Japan** *Autophagy-independent Large-scale Organelle Degradation in the Lens*
10:50	**Prof. Mingjie ZHANG** **Southern University Of Science And Technology, China** *Phase Separation in Synapse Formation and Function*
11:20	**Prof. Shaorong GAO** **Tongji University, China** *Epigenetic Regulation of Early Embryo Development and Somatic Cell Reprogramming*
11:50 – 14:00	**Poster Session I**

Day ONE: 23 July 2021 (Friday) – PM
Venue: N2 - University Hall

Onsite Session ONE - Autophagy in Health and Disease

Session Chair: Prof. Han-Ming SHEN & Prof. Jiahong LU

14:00	**Prof. Yu XUE** **Huazhong Unviersity of Science and Technology, China** *Artificial Intelligence Biology: A New Paradigm in Biomedical Sciences*
14:20	**Prof. Jun CUI** **Sun Yat-sen University, China** *The Crosstalk between Host Innate Antiviral Signaling and SARS-CoV-2 Proteins*
14:40	**Prof. Du FENG** **Guangzhou Medical University, China** *Identification of Novel Ribophagy Receptors*
15:00	**Prof. Shiqian QI** **Sichuan University, China** *The Structure and Function of ALS-linked C9orf72*
15:20	**Prof. Jiahong LU** **University of Macau, China** *Can We Slow Down Brain Ageing by Natural Autophagy Enhancers?*
15:40	**Coffee Break and Poster**

Onsite Session TWO - Genome Organization in Development and Disease

Session Chair: Prof. Edwin CHEUNG & Prof. Lijun DI

16:10	**Prof. Chunhui HOU** **Southern University of Science and Technology, China** *Three-Dimensional Folding Dynamics of the Xenopus Tropicalis Genome*
16:30	**Prof. Minglei SHI** **Tsinghua University, China** *Quantifying Liquid-Liquid Phase Separation Property of Chromatin Under Physiological Conditions*
16:50	**Prof. Guoliang LI** **Huazhong Agricultural University, China** *The Development of Digestion-Ligation-Only Hi-C and Its Application in Cervical Cancer*
17:10	**Prof. Wei XIE** (**Online) **Tsinghua University, China** *Epigenetic Inheritance and Reprogramming During Early Animal Development*

Onsite Session THREE - Stem Cells, Development and Aging

Session Chair: Prof. Ren-He XU & Prof. Guokai CHEN

17:30	**Prof. Lin LIU** **Nankai University, China** *Roles and Regulation of Telomere Length in Stem Cell Pluripotent States*
17:50	**Prof. Guotong XU** **Tongji University, China** *Treatment of Retinal Degeneration with Naive RPE Cells and Anti-EMT RPE Cells*
18:10	**Prof. Jinsong LI** (**Online) **Shanghai Institute of Biochemisty and Cell Biology, Chinese Academy of Sciences, China** *Sperm-Like Stem Cell-Mediated Genome Editing*

< END of 23 July >

Day 2: 24 July 2021 (Saturday) – AM
Venue: N2 - University Hall

08:30	嘉賓接待 Guest Reception
	Onsite Session FOUR - Recent Advance in Drug Discovery and Delivery **Session Chairs: Prof. Leo LEE & Prof. Henry KWOK**
08:40	**Prof. Xiangyang SHI** **Donghua University, China** *Intelligent Design of Nanomedicine for Ultrasound-Enhanced Tumor Theranostics*
09:00	**Prof. Yongjun DANG** (**Online) **Chongqing Medical University, China** *Target Identification and Mechanistic Study of Bioactive Compounds*
09:20	**Prof. Zhenhua LI** (**Online) **Southern Medical University, China** *Cell vesicles for the Applications in Biomedical Engineering*
09:40	**Prof. Jin-Xin BEI** (**Online) **Sun Yat-sen University, China** *Dissecting the Heterogeneity Nature of EBV-related Malignancies*
10:00	**Coffee Break and Poster**
	Onsite Session FIVE - Tumor Immunology and Immunotherapy **Session Chairs: Prof. Xin CHEN & Prof. Qi ZHAO**
10:50	**Prof. Zhe-Xiong LIAN** **South China University of Technology, China** *Hepatic CD8+ T Cells in Autoimmune Liver Diseases*
11:10	**Prof. Fubin LI** **Shanghai Jiao Tong University School of Medicine, Shanghai Institute of Immunology** *Progress in understanding Antibody Agonism– an Unnatural Mode of Action*
11:30	**Prof. Youhai CHEN** (**Online) **CAS Shenzhen Institutes of Advanced Technology, China** *New Immune Checkpoints for Cancer Therapy*
11:50	**Prof. Fan PAN** (**Online) **Chinese Academy of Sciences, China** *Targeting Regulatory T cells in Tumor Immunotherapy*
12:10	**Prof. Zhiwei CHEN** (**Online) **The University of Hong Kong, China** *Isoformic Regulation of Exhausted T Cells in Hepatocellular Carcinoma*
12:30	**Prof. Han LIU** (**Online) **Shanghai Jiao Tong University School of Medicine, Ruijin Hospital, China** *A T-cell Independent Universal Cellular Therapy Strategy*
12:50 – 14:00	**Poster Session II**

Day 2: 24 July 2021 (Saturday) – PM
Venue: N2 - University Hall

Onsite Session SIX - Neuroscience, Aging and Degenerative Diseases

Session Chair: Prof. Wenhua ZHENG & Prof. Jian-Hui LIANG

14:00	**Prof. Jian-Hui LIANG** **Peking University, China** *Role of Molecular Chaperone Hsp70 in Morphine Addiction*
14:20	**Prof. Jiangping XU** (**Online) **Southern Medical University, China** *Regulatory Mechanism of Phosphodiestase 4-mediated Signal Pathways in Parkinson's Disease*
14:40	**Prof. Wenhua ZHENG** **University of Macau, China** *The Neuronal Protective Effect of Artemisinin and Its Therapeutic Potential in Alzheimer's Disease*
15:00	**Prof. Ligang CHEN** **The Affiliated Hospital of Southwest Medical University** *Deep Brain Stimulation Robot-Assisted Surgery for Parkinson's Disease*
15:20	**Prof. Zhongshu TANG** **Sun Yat-Sen University, China** *Mechanism of Amblyopia*
15:40	**Prof. Aihua LIU** (**Online) **Capital Medical University, China** *Exosome-encapsulated microRNA-140-5p Alleviates Neuronal Injury Following Subarachnoid Hemorrhage by Regulating IGFBP5-mediated PI3K/AKT Signaling Pathway*
16:00	**Coffee Break and Poster**

Onsite Session SEVEN - Traditional Medicines and Drug Discovery

Session Chairs: Prof. Shaoping LI & Prof. Simon LEE

16:30	**Prof. Jinsong BIAN** **Southern University of Science and Technology, China** *Targeting Na+/K+ ATPase to Treat Parkinson's Disease*
16:50	**Prof. Maggie Pui-Man HOI** **University of Macau, China** *Discovery and Development of New Drug from Chinese Medicines Against Cerebrovascular and Neurodegenerative Diseases*
17:10	**Prof. Li FU** (**Online) **Jilin University & Dalian Fusheng Natural Medicine Research Institute, China** *Discovery and Development of Single Compound Chinese Medicine Ginsenoside Rg3*
17:30	**Prof. Ailin LIU** (**Online) **Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College, China** *Discovery of Drug Candidates Towards SARS-CoV-2 via Targeting Virus-Host Interactome*
17:50	**Prof. Wencai YE** (**Online) **Jinan University, China** *Bioactive Constituents and Innovative Drugs Research from the Traditional Chinese Medicine and Natural Products*
18:10	**Best Poster Awards**
18:20	**Closing**

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Online Plenary Session

Session Chair:

Prof. Chuxia DENG

23 July 2021

Prof. Lieping CHEN

United Technologies Corporation Professor in Cancer Research
Professor of Immunobiology, of Dermatology and of Medicine (Medical Oncology)
Co-Leader, Cancer Immunology, Yale Cancer Center
Yale University

Talk Title: **Immunotherapy: A New Era for Cancer Treatment**

Biography:

Lieping Chen studies cell surface proteins that control lymphocyte activation and suppression and applies these findings to treat human diseases. In 1992, his works built original concept for current efforts using costimulatory and coinhibitory molecules to enhance tumor immunity as an approach to treat human cancer. Dr. Chen co-discovered the PD-1/PD-L1 pathway and singularly established the PD-1/PD-L1 pathway as cancer immunotherapy target. He also helped initiate and organize the first-in-man clinical trial of anti-PD-1 antibody for treating human cancer and developed PD-L1 staining as a biomarker to predict treatment outcome. Dr. Chen's discoveries have revolutionized cancer treatment and led to the development of anti-PD-1/PD-L1 antibody therapy against broad spectrum of advanced human cancers. His laboratory also discovered many important immune modulation pathways (4-1BB, ICOS/B7-H2, B7-H3, B7-H4, B7-H5/CD28H, PD-1H, LIGHT/HVEM, TROY, SALM5/HVEM, Siglec-15, FGL1/Lag-3 etc.), their immunological functions and applications in human disease treatment.

Abstract:

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Prof. John MEKALANOS

Adele H. Lehman Professor of Microbiology and Molecular Genetics
Harvard Medical School

Talk Title: Protein Covariance Networks Reveal Interactions Important to the Emergence of Viral and Bacterial Pathogens

Biography:

Dr. John Mekalanos is Professor of Microbiology at Harvard Medical School. He received his PhD at the University of California in 1978 and after postdoctoral training at Harvard joined the Department of Microbiology and Molecular Genetics in 1981 as an assistant professor and was promoted to full professor in 1986. He also served as chair of the Department of Microbiology and Immunobiology for twenty years (1996-2016). Dr. Mekalanos' research investigates multiple facets of bacterial pathogenesis, with an emphasis on using functional genomics to explore pathogen-host interactions, virulence regulation, and antibiotic target identification. One of the important practical benefits of this research has been the development of live attenuated vaccines effective against cholera and the discovery of the first anti-virulence drug (virstatin). He was elected to the National Academy of Sciences in 1998. Dr. Mekalanos has been a member of the FDA Advisory Committee on Vaccines and Related Biologics and has also advised numerous governmental and private agencies including the National Institutes of Health, the World Health Organization, etc. Dr. Mekalanos has co-founded two biotechnology firms that are now publically traded (Avant Immunotherapeutics and PharmAthene). In summary, John Mekalanos is one of world's most pre-eminent microbiologists. His research and mentoring of trainees have literally created and continue to define the landscape of the microbiology. He is the ideal choice for the ASM Lifetime Achievement Award.

Abstract:

SARS-CoV-2 is one of three recognized coronaviruses (CoVs) that have caused epidemics or pandemics in the 21st century and that likely emerged from animal reservoirs based on genomic similarities to bat and civet viruses. We have performed an analysis of conserved interactions between amino acid residues in core proteins encoded by SARS-CoV-related beta-coranaviruses. We identified pairs and networks of residue variants that exhibited statistically high frequencies of covariance with each other. While these interactions are likely key to both protein structure and other protein-protein interactions, we have also found that they can be used for understanding viral evolution and adaptation. Our data provide evidence that the evolutionary processes that converted a bat virus into human pathogen was in part driven by covariant residues that reside in viral proteins that include S and the 3a viroporin. We conclude that recombination between CoVs is likely followed by adaptive mutations in networks of covariant amino acids that affect receptor binding and viral pathogenesis in ways that lead to enhanced transmission in the human host. These insights could inform therapeutic and vaccine development for this extremely important class of zoonotic viruses. We then expanded covariant analysis to the gene-protein level in order to study the evolution of bacterial pathogens. We applied a correlation-based approach called **P**rotein **Co**variation **A**nalysis)(or PCoVA) to the *Vibrio cholerae* pangenome to reveal networks of predicted positive and negative genetic relationships. This comprehensive PCoVA dataset for *V. cholerae* identified all known *V. cholerae* virulence genes within one single network that also included many additional uncharacterized genes that likely influence host colonization, disease, and transmission. The PCoVA computational approach can be applied to any taxon where phenotypes of interest are well-defined within a set of diverse but related strains. In sum, we developed a bioinformatics pipeline called PCoVA that incorporates correlative methods that leverages the entire gene content of related strains to predict gene compatibilities and incompatibilities that likely drives the emergence as pandemic bacterial pathogens or even commensal pathobionts associated with specific disease states.

Prof. Noboru MIZUSHIMA

Professor
Graduate School and Faculty of Medicine
The University of Tokyo, Japan

Talk Title: **Autophagy-Independent Large-Scale Organelle Degradation in the Lens**

Biography:

Prof. Noboru Mizushima is the Professor of the Department of Biochemistry and Molecular Biology, Graduate School of Medicine, The University of Tokyo. Prof. Mizushima was awarded the Medal of Honor with Purple Ribbon and received the “Minister of MEXT Award” at the 4th Award Ceremony for the Japan Medical Research and Development Grand Prize and the “Medical Award” of the Japan Medical Association. Prof. Mizushima was selected as a 2020 Clarivate Analytics Highly Cited Researcher (7th straight year). His laboratory is working on the intracellular degradation systems, particularly focusing on the molecular mechanisms and physiological significance of autophagy.

Abstract:

The lens is composed of fiber cells that undergo massive degradation of all organelles during terminal differentiation. However, the mechanism of organellar degradation remains largely unknown. We previously showed that this process is independent of macroautophagy. To identify a novel autophagy-independent mechanism of organelle degradation in the lens, we established a live imaging system of this process in zebrafish and found that matrix proteins of the ER and mitochondria were released into the cytosol during differentiation, indicating that these organelles are ruptured. By transcriptome and CRISPR/Cas9 knockout screens, we revealed that PLAAT (phospholipase A and acyltransferase) family phospholipases, which are highly expressed in the lens, are essential for the degradation lens organelles such as the ER, mitochondria, and lysosomes in zebrafish and mice. PLAATs translocate from the cytosol to these organelles to degrade them. The translocation of Hrasls to organelles depends on the differentiation of fiber cells and damage to organelle membranes, both of which are regulated by Hsf4. PLAAT-mediated organelle degradation is essential for achieving optimal transparency and refractive function of the lens. These findings expand our understanding of intracellular organelle degradation and provide insights into the mechanism by which vertebrates acquired transparent lenses.

Prof. Mingjie ZHANG

Dean
School of Life Sciences
Southern University of Science and Technology

Talk Title: **Phase Separation in Synapse Formation and Function**

Biography:

Before becoming the Founding Dean of the School of Life Sciences, Southern University of Science and Technology (SUSTech) at the end of 2020, Prof Zhang was a Kerry Holdings Professor of Science, Senior Fellow of the Institute for Advanced Study, and Chair Professor in the Division of Life Science, HKUST. Research in Prof. Zhang's laboratory has been focusing on two areas in the past 20 years. The first area concerns the structural and biochemical basis of neuronal signaling complex organization by scaffold proteins. The second area is how neurons develop polarity during their development and maintain the polarity in their adulthood. He has authored more than 200 research articles in the prestigious scientific journals including Science, Cell, Mol Cell, Nature Structural & Molecular Biology, Neuron, Nature Neuroscience, Nature Chemical Biology, Developmental Cell, PNAS, EMBO J, etc. Their breakthrough discoveries on phase separation-mediated synapse formation and function have far reaching implications in basic as well as translational research in neuroscience. About 20 PhD graduates and postdoctoral fellows trained in his lab have established their independent research groups around the world.

Abstract:

Emerging evidence indicates that liquid-liquid phase separation, the formation of a condensed molecular assembly within another diluted aqueous solution, is a means for cells to organize highly condensed biological assemblies with broad functions and regulatory properties in different subcellular regions. Molecular machineries dictating synaptic transmissions in both presynaptic boutons and postsynaptic densities of neuronal synapses are such biological condensates. In this talk, I will present our recent work showing how phase separation can build dense synaptic molecular clusters, highlight unique features of such condensed clusters in the context of synapse formation and plasticity, and discuss how aberrant phase-separation-mediated synaptic assembly formation may contribute to dysfunctional signaling in psychiatric disorders.

Prof. Shaorong GAO

Professor

Institute for Regenerative Medicine, Shanghai East Hospital, Shanghai Key Laboratory of Signaling and Disease Research, Frontier Science Center for Stem Cell Research, School of Life Sciences and Technology, Tongji University

Talk Title: **Epigenetic Regulation of Early Embryo Development and Somatic Cell Reprogramming**

Biography:

Dr. Shaorong Gao is currently a full professor and the dean for the School of Life Sciences and Technology, Tongji University, Shanghai, China. Dr. Shaorong Gao received the Doctorate degree in Reproductive Biology from the Institute of Zoology, Chinese Academy of Sciences. He then did post-doc in UK and US focusing on somatic cell reprogramming. He returned to China in late 2005 and joined the National Institute of Biological Sciences (NIBS) as a principal investigator. In 2013, he moved to Tongji University and became the dean for School of Life Sciences and Technology. The research projects in his laboratory focus on dissecting the epigenetic regulation mechanism in early embryo development and somatic cell reprogramming. He has published over 150 research papers in prestigious scientific journals including *Nature*, *Science*, *Nature Genetics*, *Cell Stem Cell* etc.

Abstract:

Epigenetic reprogramming plays important roles in creating a totipotent embryo from terminally differentiated gametes, and as well as in reprogramming of somatic cells to totipotent/pluripotent state. In this talk, I'll briefly summarize the recent progress that we achieved in understanding the mechanism of epigenetic reprogramming in normal embryo development and somatic cell reprogramming. In particular, the regulation and role of histone modifications and DNA methylation as well as RNA methylation in early embryo development and somatic cell reprogramming will be discussed.

Session ONE

Session Chair:

Prof. Han-Ming SHEN

Session Title:

Autophagy in Health and Disease

23 July 2021

Prof. Yu XUE

Professor

Huazhong Unviersity of Science and Technology

Talk Title: **Artificial Intelligence Biology: A New Paradigm In Biomedical Sciences**

Biography:

Dr. Yu Xue is a professor at the Department of Bioinformatics & Systems Biology, Center for Artificial Intelligence Biology, College of Life Science and Technology of Huazhong University of Science and Technology. His major interests are focused on the development of novel databases, AI algorithms and computational software packages, such as GPS (Group-based Prediction System) series algorithms and a novel deep learning framework named Hybrid Learning, for understanding the temporally and spatially regulatory roles of proteins and post-translational modifications (PTMs) involved in cellular signaling pathways and networks, by combining systems biology, bioinformatics, and molecular & cellular biology approaches to identify functional regulators and PTM events in autophagy and human cancer. Dr. Xue has published 100 papers in a number of high-profile journals, such as Immunity, Nature Biomedical Engineering, Nature Communications, and Nature Protocols, with > 8000 citations. He is an associate Editor of Science Bulletin, Genomics, Proteomics & Bioinformatics, Cells, BMC Genomics, Scientific Reports and PLoS ONE. He is quite active on pushing the communication and collaboration of young bioinformaticians in China. ResearcherID: https://publons.com/researcher/G-5929-2011/.

Abstract:

Recent advances in machine learning have provided a great opportunity to accurately infer the complex causality from big biological data, and boomed the establishment of a new interdisciplinary field named artificial intelligence biology (AIBIO). Here, we reported our recent progresses in AIBIO for analysis of autophagy selectivity. First, we hypothesize that a subset of human cancer mutations may alter autophagy selectivity through impacting the LC3-interacting region (LIR) motif, a major sequence determinant of cargo recognition. Then, we develop an integrative pipeline named inference of cancer-associated LIR-containing proteins (iCAL), which integrates a machine learning-based algorithm named prediction of the LIR motif (pLIRm), a model-based algorithm named pLAM to predict LIR motif-associated mutations (LAMs), a pan-cancer analysis, and cell- and animal-based validations. Using iCAL, we have identified 148 LIR-containing proteins (LIRCPs) that carry single point mutations within the LIR motif, including some well-established autophagy-related (ATG) genes and autophagy regulators as well as many novel candidate genes. Among these candidate genes, we functionally confirm that starch-binding domain-containing protein 1 (STBD1), a gene involved in transporting glycogen to lysosomes, has a previously unappreciated role in suppressing cancer growth. Mechanistically, STBD1 inhibits tumor growth via metabolic reprogramming in cancer cells, including rewiring glycolysis and the pentose phosphate pathway. This work suggests that altered autophagy selectivity is a frequently-used mechanism by cancer cells to survive during various stresses, and provides a framework to discover additional autophagy-related pathways that influence carcinogenesis. The source codes of pLIRm and pLAM are freely available at: https://github.com/BioCUCKOO/pLIRm-pLAM.

Prof. Jun CUI
Professor
Sun Yat-sen University

Talk Title: The Crosstalk Between Host Innate Antiviral Signaling and Sars-Cov-2 Proteins

Biography:

Jun Cui received his PhD degree in Biology from Nanjing University, China in 2009. After his postdoctoral research at Baylor College of Medicine and the Institute of Methodist Hospital, he joined Sun Yat-sen University as a Full Professor of Biochemistry in 2012 and has been the dean of the Department of Biochemistry since 2015. His research interests include the activation, regulation, and disease relevance of innate immune signaling.

Abstract:

The recent widespread epidemic of SARS-CoV-2 infection has led to a pressing need for comprehensive understanding of the molecular pathogenesis of SARS-CoV-2 to aid in the development of effective vaccines and antiviral therapies. However, little is known about pathogenesis of SARS-CoV-2 and the confrontation between host and the virus. Recently we have discovered several novel mechanisms of SARS-CoV-2 antagonizing host antiviral immunity by targeting the cross-talk of type I interferon (IFN) induction, JAK-STAT pathway and inflammation network.

Prof. Du FENG

Professor
Guangzhou Medical University

Talk Title: **Identification of Novel Ribophagy Receptors**

Biography:

Dr. Feng is a Professor in State Key Laboratory of Respiratory Diseases and Associate Dean in School of basic medical sciences, Guangzhou Medical University, Dr. Feng obtained PhD at Tsinghua University, and completed his postdoc training at Harvard Medical School. His lab focuses on selective autophagy and is developing new protac molecules in treating cancer. He identified a novel mitophagy receptor and characterized the signaling pathway of this receptor.

Abstract:

Ribosomes are very abundant in the cell and it accounts for about 3-6% of the total intracellular mass in terms of protein. When cells are under stressful conditions such as nutrient deprivation, on the one hand, some ribosomes are shut down to terminate the synthesis of most new proteins, and on the other hand, excess ribosomes are degraded to feed the cell by initiating ribosomal autophagy. Previous studies reported that NUFIP1 is a ribosomal autophagy receptor that mediates the autophagic degradation of ribosomes under starvation conditions (SCIENCE, 2018), but since ribosomes are a huge molecular machine with a large surface area, we believe that other ribosomal autophagy receptors may exist. Using GST-LC3 as a bait, we incubated purified ribosomes under normal and starvation conditions with GST-LC3 and the specific LC3-binding proteins RPS2 and RPS3A; further studies revealed that under starvation conditions, these proteins undergo nucleoplasmic translocation and co-localize with LC3; immunoprecipitation and GST-pulldown experiments confirmed that both proteins interact with LC3 and ribosomes and contain the classical LC3 interaction region: LIR, while mutation or deletion of the LIR region can significantly weaken their interactions. We further found that under starvation conditions, these proteins underwent nucleoplasmic translocation and co-localized with LC3; immunoprecipitation and GST-pulldown experiments confirmed that both proteins interacted with LC3 and ribosomes and contained the classical LC3 interaction region: LIR, while mutation or deletion of the LIR region significantly weakened their interactions . Knockdown of these proteins significantly inhibited starvation-induced ribosomal autophagy and reduced cell survival under starvation conditions. In conclusion, our study is likely to identify new ribosomal autophagy receptors.

Prof. Shiqian QI

Professor
Sichuan University

Talk Title: **The Structure and Function of Als-Linked C9Orf72**

Biography:

Dr. Qi receveid his Bachelor in Biology in College of Life Science, Shandong University and PhD in Molecular and Structural Biology in School of Life Science, Tsinghua University. He was a Visiting Scholar Fellow in James Hurley Lab at NIH from October, 2011 to 2013 and Postdoctoral Fellow in James Hurley Lab at UC Berkeley from August 2013 until now. He is a PI at the State Key Lab in the West China Hospital, Sichuan University, since July, 2016. His research interests are: i.) Study of the mechanism of which α-Arrestin proteins participate in the regulation of receptors on membrane by biochemical, biophysical and crystallographic methods; ii.) Study the function and structures of the proteins and protein complexes which mediate the pathogenic microbe invasion of and release from host cells and iii.) Explore the molecular mechanism how proteins/protein complexes participate in autophagy.

Abstract:

A massive intronic hexanucleotide repeat (GGGGCC) expansion in C9ORF72 is a genetic origin of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Recently, C9ORF72, together with SMCR8 and WDR41, has been shown to regulate autophagy and function as Rab GEF. However, the precise function of C9ORF72 remains unclear. Here, we report the cryo-EM structure of the human C9ORF72-SMCR8-WDR41 complex at a resolution of 3.2 Å. The structure reveals the dimeric assembly of a heterotrimer of C9ORF72-SMCR8-WDR41. Notably, the C-terminal tail of C9ORF72 and the DENN domain of SMCR8 play critical roles in the dimerization of the two protomers of the C9ORF72-SMCR8-WDR41 complex. In the protomer, C9ORF72 and WDR41 are joined by SMCR8 without direct interaction. WDR41 binds to the DENN domain of SMCR8 by the C-terminal helix. Interestingly, the prominent structural feature of C9ORF72-SMCR8 resembles that of the FLNC-FNIP2 complex, the GTPase activating protein (GAP) of RagC/D. Structural comparison and sequence alignment revealed that Arg147 of SMCR8 is conserved and corresponds to the arginine finger of FLCN, and biochemical analysis indicated that the Arg147 of SMCR8 is critical to the stimulatory effect of the C9ORF72-SMCR8 complex on Rab8a and Rab11a. Our study not only illustrates the basis of C9ORF72-SMCR8-WDR41 complex assembly but also reveals the GAP activity of the C9ORF72-SMCR8 complex.

Prof. Jiahong LU

Professor
State Key Laboratory of Quality Research in Chinese Medicine
Institute of Chinese Medical Sciences
University of Macau

Talk Title: **Can We Slow Down Brain Ageing By Natural Autophagy Enhancers?**

Biography:

Dr. Lu got his PhD in Hong Kong Baptist University. He spent 3 years in Icahn School of medicine at Mount Sinai for postdoctoral training before joining University of Macau as an assistant professor. Dr. Lu's major research interests are autophagy in human diseases and pharmacological study on traditional Chinese medicine. Dr. Lu has published a series of papers as first author or corresponding author in high profile journal including: Nature Communications, Autophagy (5), Molecular neurodegeneration, Cell death and disease (2), Pharmacological research, etc. with a total citation of over 5,000 times (WoS).

Abstract:

Autophagy is a bulk degradation process for recycle of cellular content. Damaged or aggregated protein and aged organelles can be degraded by autophagy. Neurodegenerative diseases including Alzheimer's disease and Parkinson's disease are featured by accumulation of aggregation prone proteins in the brain. Dysregulation of autophagy has been observed in the biopsy samples from patients. Enhancing autophagy by natural autophagy inducers can be a novel strategy fighting against neurodegenerative diseases.

Session TWO

Session Chair:

Prof. Edwin CHEUNG

Session Title:

Genome Organization in Development and Disease

Theme:

Genome Biology

23 July 2021

Prof. Chunhui HOU

Associate Professor
College of Science
Southern University of Science and Technology

Talk Title: **Three-Dimensional Folding Dynamics of the Xenopus Tropicalis Genome**

Biography:

Dr. Hou graduated from Fudan University with BS degree in 1997 and received his PhD degree in 2004 from Chinese Academy of Sciences. The he was a Visiting fellow in Dr. Ann Dean's lab in NIDDK, NIH from 2004 to 2009 and Postdoctoral fellow in Dr. Victor Corces' lab in Emory University from 2009 to 2013. He is now a Associate professor in the Department of Biology, SUSTech since 2013.

Abstract:

Metazoan interphase chromosomes are organized into topologically associating domains (TADs), characterized by regions of elevated self-interactions. However, our understanding of how TADs are initiated remains incomplete. Herein, we combined single-molecule sequencing, high-throughput chromosome conformation capturing (Hi-C), and gene silencing to obtain detailed insights into TAD formation in Xenopus tropicalis embryos. First, TAD formation in X. tropicalis is similar to mice and flies, but distinct from humans and does not depend on the transcriptional activation of the zygotic genome despite their co-occurrence. This process is followed by further refinements in active and repressive chromatin compartments and the formation of loops and stripes. Second, within TADs, higher self-interaction frequencies at one end of the boundary are associated with higher DNA occupancy of architectural proteins CTCF and Rad21. Third, similar to CTCF and Rad21, the chromatin remodeling factor ISWI is required for de novo TAD formation. Finally, TAD structures can be highly variable in different tissues. In summary, our work shows that X. tropicalis is a powerful model for chromosome architecture analysis and suggests chromatin remodeling plays an essential role in de novo TAD establishment.

Prof. Minglei SHI

Research Assistant Professor
MOE Key Laboratory of Bioinformatics
Bioinformatics Division, BNRIST & School of Medicine
Tsinghua University

Talk Title: Quantifying Liquid-Liquid Phase Separation Property of Chromatin Under Physiological Conditions

Biography:

Dr. Minglei Shi has been engaged in three-dimensional genome (3DG) research for a long time, with particular attention to the important role of protein in 3DG. He successively applied ChIA-PET, Hi-ChIP, IF-FISH and other sequencing and imaging methods to study 3DG mediated by specific proteins. In recent years, Dr. Minglei Shi has integrated proteomics and 3DG to develop a multi-omics research technology Hi-MS. Hi-MS can capture many DNA binding proteins at one time, and can quantitatively measure the liquid-liquid phase separation property of the chromosome associated proteins, which greatly enriches people's understanding of the role of phase separation in the regulation of gene expression.

Abstract:

Liquid–liquid phase separation (LLPS) is an important organizing principle for biomolecular condensation and chromosome compartmentalization. However, while many proteins have been reported to undergo LLPS, quantitative and global analysis of chromatin LLPS property remains absent.

By combing chromatin associated protein pull-down, quantitative proteomics and 1,6-hexanediol treatment, we developed Hi-MS and defined anti-1,6-HD index of chromatin-associated proteins (AICAP) to quantitative measurement of LLPS property of chromatin-associated proteins in their endogenous state and physiological abundance. The AICAP values were verified by previously reported experiments and were reproducible across different MS platforms. Moreover, the AICAP values were highly correlate with protein functions. Proteins act in active/regulatory biological process often exhibit low AICAP values, while proteins act in structural and repressed biological process often exhibit high AICAP values.

We further revealed that chromatin organization changes more in compartment A than B, and the changes in chromatin organization at various levels, including compartments, TADs and loops are highly correlated to the LLPS properties of their neighbor nuclear condensates.

Our work provided the first global quantitative measurement of LLPS properties of chromatin-associated proteins and higher-order chromatin structure, and demonstrate that the active/regulatory chromatin components, both protein (trans) and DNA (cis), exhibit more hydrophobicity-dependent LLPS properties than the repressed/structural chromatin components.

Prof. Guoliang LI

Professor
College of Life Science and Technology
Huazhong Agricultural University

Talk Title: The Development of Digestion-Ligation-Only Hi-C and Its Application In Cervical Cancer

Biography:

Dr. Guoliang Li is a professor in Bioinformatics and vice dean, College of Informatics, Huazhong Agricultural University, Wuhan, China. He got his PhD degree in Computer Science from School of Computing, National University of Singapore, Singapore in 2009. He worked as a post-doc and research associate in Genome Institute of Singapore in 2009-2012, and worked as a research scientist in Jackson Laboratory for Genomic Medicine in 2013. He jointed Huazhong Agricultural University, Wuhan, China in 2014. He has published 80+ peer-reviewed papers, including co-first-authored papers in Cell and Nature Genetics and one paper in Nature Genetics as co-correspondence author. His main research interests are epigenomics, bioinformatics, and three-dimensional (3D) genomics, especially in long-range chromatin interactions.

Abstract:

Chromosome conformation capture technologies open an avenue to investigate the three-dimensional (3D) structures of genomes. In order to improve the efficiency of the Hi-C method, we developed a simple Digestion-Ligation-Only Hi-C (DLO Hi-C) technology, which requires only two rounds of digestion and ligation without biotin-labeling and pull-down for reducing the cost. The noise DNA was efficiently removed in a cost-effective step by purifying specific linker-ligated DNA fragments. We have applied DLO Hi-C method to a patient sample with integration of human papillomavirus (HPV). Molecular analyses showed that chromosome 19 was enriched with genome variation and differential expression densities, and a correlation between 3D structural change and gene expression. More importantly, HPV integration divided one topologically associated domain (TAD) into two smaller TADs and hijacked an enhancer from PEG3 to CCDC106, with expression decrease in PEG3 and expression increase in CCDC106. This expression dysregulation was further confirmed using 10 samples exhibiting the same HPV-CCDC106 integration from our cohort. In summary, we found that HPV-CCDC106 integration tended to alter the architecture of local chromosome and hijacked an enhancer via 3D genome structure remodeling, thus providing insight into the 3D structural mechanism underlying HPV integration in cervical carcinogenesis.

*The main collaborators are Dr. Gang Cao (gcao@mail.hzau.edu.cn) and Dr. Peng Wu (pengwu8626@tjh.tjmu.edu.cn).

Prof. Wei XIE

Professor
School of Life Sciences
Tsinghua University

Talk Title: **Epigenetic Inheritance and Reprogramming During Early Animal Development**

Biography:

Dr. Wei Xie is a Professor at School of Life Sciences, Tsinghua University, and an HHMI International Research Scholar. Using interdisciplinary approaches, Dr. Xie is dedicated to understanding how the life clock is reset after fertilization by reprogramming the epigenomes in animal early development. His group established a series of ultra-sensitive technologies to analyze chromatin dynamics using only several hundred cells or fewer. By doing so, his team revealed how chromatin accessibility, histone modifications, and 3D chromatin architecture are re-configured during early mammalian development. Such epigenetic reprogramming is essential for successful parental-to-zygotic transition and the ultimate generation of a totipotent embryo.

Abstract:

Drastic epigenetic reprogramming and global transcription controls occur during mammalian early embryogenesis. Deciphering the molecular events underlying these processes is crucial for understanding how parental-to-zygotic transition occurs and how life really begins. Probing these questions was previously hindered by the scarce experimental materials that are available from early embryos. By developing a set of ultra-sensitive chromatin analysis technologies, we probed chromatin reprogramming during early mouse development for chromatin accessibility, histone modifications, and 3D architecture. These studies unveiled highly dynamic and non-canonical chromatin regulation during parental-to-zygotic transition and zygotic genome activation (ZGA). Recently, we also investigated how the core transcription machinery participates zygotic genome activation (ZGA) in mouse early embryos. In this talk, I will discuss our recent findings related to epigenetic reprogramming and transcription regulation in early embryos, and how these discoveries further our understanding on how life starts after fertilization.

Session THREE

Session Chair:

Prof. Ren-He XU

Session Title:

Stem Cells, Development and Aging

Theme:

Stem Cell, Gene & Cell Therapy

23 July 2021

Prof. Liu LIN

Professor
College of Life Sciences
Nankai University

Talk Title: **Roles and Regulation of Telomere Length in Stem Cell Pluripotent States**

Biography:

Liu Lin, PhD, professor of Nankai University. Main research directions: 1) The role and regulation mechanism of telomeres and heterochromatin in pluripotent stem cell pluripotency and somatic cell reprogramming, tumorigenesis and recurrence; 2) Ovarian aging mechanism and new strategies for anti-ovarian aging . Presided over a number of major national projects, including national key research and development plans, national major scientific research plans, national international scientific and technological cooperation projects, national natural science foundation committee key and major research projects, and the Tianjin "stem cell and regenerative medicine" innovation team takes the lead People wait. Won a number of awards and honors, including the "Changjiang Scholars Award Program" Distinguished Professor of the Ministry of Education, the National Outstanding Youth Fund, the "Middle-aged and Young Experts with Outstanding Contributions" of the National Ten Thousand Thousand Talent Project, the first prize of Assisted Reproductive Technology of the American Society of Reproductive Medicine. Served as a reviewer and editorial board member of many international scientific journals, including Science Bulletin, Signal Transduction and Targeted Therapy, Frontiers in Oncology, J Assist Reprod Genet, etc. Authored more than 150 papers in international journals.

Abstract:

Pluripotency and genomic stability are major determinants for effective and safe applications of pluripotent stem cells (PSCs) in eventually clinic based stem cell therapy and regenerative medicine. It has been generally assumed that PSCs possess high telomerase activity and longer telomeres, in contrast to somatic cells. Naïve and primed PSCs represent two different pluripotent states. Primed PSCs following *in vitro* culture exhibit lower developmental potency as evidenced by failure in germline chimera assays, unlike mouse naïve PSCs. However, the molecular mechanisms underlying the lower developmental competency of primed PSCs remain elusive. We examined the regulation of telomere maintenance, retrotransposon activity, and genomic stability of primed PSCs and compared them with naïve PSCs. Surprisingly, primed PSCs only minimally maintain telomeres, with increased telomere fragility, in association with declined DNA recombination and repair activity, in contrast to naïve PSCs that robustly elongate telomeres. Notably, genomic instability of primed PSCs is increased, and this is attributable to aberrant retrotransposon activity. Our data suggest that the telomere fragility and retrotransposon-induced genomic instability together with declined DNA recombination repair may link to compromised developmental potency of primed PSCs, noticeably distinguishable from naïve PSCs. Conventional human ESCs resemble mouse primed PSCs, and thus likely also show lower developmental potency, but unfortunately due to ethic issues, functional tests of pluripotency for mice cannot be equally applied to humans. Extensive efforts on ESCs have been put to convert primed into extended or ground naïve state. But it is critical to scrutinize the telomere and genomic stability in extended naïve ESCs.

Prof. Guo-Tong XU

Professor
Pharmacology and Ophthalmology
School of Medicine
Tongji University

Talk Title: **Treatment of Retinal Degeneration With Naive Rpe Cells and Anti-Emt Rpe Cells**

Biography:

Professor Xu received his MD degree from Peking Union Medical College (China) and PhD degree from University of North Texas (USA) in the 90's. Following several years of postdoctoral training at both NIH and Alcon Lab. in the States, he moved back to China in 1997, and served as the director of Nanjing Rainbow EyeCare Center, the China Country Director of ORBIS Flying Eye Hospital, and PI in the Institute of Health Sciences, Chinese Academy of Sciences. Currently, Dr. Xu is a professor of Pharmacology and Ophthalmology, Tongji University School of Medicine and Executive Dean of Tongji University Jiren School. He also serves as the Director of Tongji Eye Institute, and the Director of the East China Stem Cell Bank. He was the PIs for several national major projects, and the Founder President of the China Society for Stem Cell Biology. His lab has been focusing on translational study of age-related eye diseases, aging and anti-aging agent development.

Abstract:

The treatments of age-related macular degeneration (AMD) with retinal pigment epithelial (RPE) cells derived from embryonic stem cells (ESC-RPEC) and induced pluripotent stem cells (iPSC-RPEC) have been reported for many years, but the treatments could not be promoted well in clinic. The key obstacle is not the safety but the uncertain efficacy. The major factors affecting the therapeutic effects are either the donor cells, or the poor niche in the retina of the patients, or both. To improve the effects, we compared a variety of stem cells and developed two strategies to improve the RPE cells both showed remarkably enhanced efficacy. Firstly, we established an efficient method to induce ESC and iPSC to differentiate into RPE cells, and compared the therapeutic effects between naive and mature RPE cells in the process of differentiation. The results showed that the naive RPE cells, not established all the functions of mature RPE cells yet, showed stronger retinal protection in RCS rats. Its mechanisms involved the high expression of cell cycle related genes and extracellular matrix related genes so that these cells were more likely to adhere to the culture dish and form intercellular junctions. Secondly, we reprogrammed the dedifferentiated human iPSC-RPECs with the combination of retinal development related transcription factors (TFs) to produce inducible RPE cells (iRPECs), which showed a more persistent intervention on retinal degeneration than mature iPSC-RPECs. The mechanism involves that TFs regulates EMT related factors and polarity related proteins, maintains the epithelial characteristics and polarity of iRPEC, and enables the iRPECs to acquire the characteristics of anti-TGF-β-induced EMT. In the *in vivo* experiments, regulating c-myc by a Tet-on system could maintain the safety of the transplanted iRPECs while they played an anti-EMT role. Our results show that, in the harsh microenvironment of retinal degenerative eye, the naive RPECs and the iRPECs with anti-EMT could improve the function of Bruch membrane by increasing donor cells and antagonizing TGF-β-induced EMT, improve the attachment of donor cells or maintain epithelial characteristics and function, and improve the therapeutic effect in animal models. It is expected to provide an improved RPE cell line for the treatment of retinal degeneration.

Prof. Jingsong LI

Professor
Shanghai Institute of Biochemisty and Cell Biology
Chinese Academy of Sciences

Talk Title: **Sperm-Like Stem Cell-Mediated Genome Editing**

Biography:

Dr. Li obtained his PhD degree from Institute of Zoology, Chinese Academy of Sciences, in 2002 and followed by postdoctoral training at Rockefeller University before joining SIBCB in 2007. His research mainly focuses on stem cells and embryonic development. He has made fundamental contributions to the establishment of androgenetic haploid embryonic stem cells (also termed “artificial spermatids”) that can be used as sperm replacement for efficient production of semi-cloned mice (so called semi-cloning (SC) technology). Dr. Li has made great efforts to promote the applications of SC technology and shown that it can be used as a unique tool for genetic analyses in mice, including efficient generation of mouse models carrying defined point mutations related to human developmental defects; one-step generation mouse models that mimic multiple genetic defects in human diseases; and medium-scale targeted screening of critical genes or critical nucleotides of a specific gene involved in a developmental process. Most recently, Dr. Li initiated and is promoting a huge project to tag every protein in mice based on “artificial spermatid”-mediated SC technology (genome tagging project, GTP), which may enable the precise description of protein expression and localization patterns, and protein–protein, protein–DNA and protein–RNA interactions in development/ aging, physiological and pathological conditions.

Abstract:

From androgenetic haploid blastocysts derived by injection of sperm into enucleated oocytes, we generated mouse androgenetic haploid embryonic stem cells (AG-haESCs) that can support full-term embryonic development upon injection into oocytes, leading to the production of semi-cloned (SC) mice (semi-cloned technology). However, one major drawback of this technology is the very low birth rate of healthy SC mice (2% of total SC embryos transferred). Recently, we established AG-haESCs carrying H19-DMR and IG-DMR deletions (DKO-AG-haESCs) that can efficiently support the generation of SC pups at a rate of 20% (“sperm-like stem cell”). Sperm-like stem cell-mediated SC technology, combined with CRISPR-Cas9 technologies, enables one-step generation of mouse models that mimic multiple gene dosage reduction in human Myotonic Dystrophy type 1 (DM1); identification of novel mutations involved in human neural tube defects; medium-scale targeted screening of critical factors involved in bone development; base mutagenesis of a specific protein-coding gene to identify critical amino acids for protein function *in vivo*; and efficient generation of mice carrying tagged proteins at genome-scale (Genome Tagging Project, GTP). Moreover, we established haploid ESCs from monkey and human parthenogenetic embryos and most recently human artificial spermatids from androgenetic embryos. In summary, haESCs provide powerful tools for genetic analyses in mammals at both cellular and organismal levels.

Session FOUR

Session Chair:

Prof. Leo LEE &
Prof. Henry KWOK

Session Title:

Recent Advance in Drug Discovery and Delivery

Theme:

Cancer Research, Drug development & Diagnostics

24 July 2021

Prof. Xiangyang SHI

Professor
College of Chemistry, Chemical Engineering, and Biotechnology
Donghua University

Talk Title: **Intelligent Design of Nanomedicine for Ultrasound-Enhanced Tumor theranostics**

Biography:

Xiangyang Shi obtained his PhD degree in 1998 from the Chinese Academy of Sciences. From 2002 to 2008, he was appointed as a research fellow, research associate II, research investigator, and research assistant professor in Medical School of University of Michigan, Ann Arbor. In September 2008, he joined Donghua University as a full professor. He has published 415 peer-reviewed SCI-indexed journal articles with an h-index of 74. His current research interests are focused on the development of organic/inorganic hybrid nanoplatforms and dendrimeric nanoparticles for sensing, imaging, and theranostic applications, in particular for precision cancer imaging and therapy.

Abstract:

Recently, nanomedicine has been regarded as a promising tool to deliver therapeutic agents or imaging contrast agents to tumors. It is urgent to combine nanomedicines with advanced technology to overcome the obstacles in biological systems, thus achieving effective delivery of nanomedicines. Ultrasound (US) can be used in biomedical applications due to its safety, non-invasiveness, and non-ionizing radiation characteristics. In particular, ultrasound-targeted microbubble destruction (UTMD) technology that can create numerous small holes on the cell membrane via a cavitation effect has been explored to promote the delivery of nanomedicines. Herein, we designed several intelligent nanomedicines for US-enhanced tumor theranostics including dendrimer-entrapped gold nanoparticles (Au DENPs) for co-delivery of gemcitabine (Gem) and miR-21 inhibitor (miR-21i) for combination chemo and gene therapy of pancreatic tumor model, yellow fluorescent carbon dot (y-CD)/dendrimer nanohybrids loaded with efflux inhibitor D-α-tocopheryl polyethylene glycol 1000 succinate (TPGS) and anticancer drug doxorubicin (DOX) for enhanced fluorescence imaging and chemotherapy of multidrug resistance (MDR) breast tumors, and a “one-for-all” theranostic platform based on phosphorus dendrimer-copper(II) complex (1G3-Cu) for enhanced T1-weighted magnetic resonance (MR) imaging and chemotherapy of tumors. Overall, intelligent nanomedicine can be designed for US-enhanced tumor theranostics, thus providing many opportunities for further development for translational medicine applications.

Prof. Yongjun DANG

Distinguished Professor
Center for Novel Target and Therapeutical Intervention (CNTTI)
Chongqing Medical University

Talk Title: **Target Identification and Mechanistic Study of Bioactive Compounds**

Biography:

Dr. Yongjun Dang is the Distinguished Professor and the Director of the Center of New Target and Chemical Intervention of the Institute of Life Sciences of Chongqing Medical University. Before this, he was a Postdoctoral Fellow and a Research Assistant in the Department of Pharmacology and Molecular Sciences, School of Medicine, Johns Hopkins University in 2004-2010 and 2010-2012. Then he became a Professor in the Department of Biochemistry and Molecular Biology, School of Basic Medicine Sciences, Fudan University in 2012-2020. His research focusses on the Target Discovery of Diseases and Therapeutical Intervention.

Abstract:

Identification of the biological efficacy targets and the mode of action of bioactive compounds is very important and will guide future drug development and innovation. However, the strategy and techniques for target identification are still limited. Here several examples of target identification of natural products using a different strategy are discussed. 1. Celastrol has been reported the thermogenesis efficacy through inducing brown-like adipocytes in WAT, however its direct protein target and mechanism remain unclear. Here we identify GSTM1 as a critical regulator of adipocyte browning and as a target of celastrol, underscoring therapeutic potential of ethacrynic acid and celastrol in mitigating obesity and related metabolic imbalance and morbidities in humans . 2. Grincamycins are a class of marine-derived antibiotics that have potent antitumor activities. Through a multi-omics strategy, we identify isocitrate dehydrogenase 1(IDH1) is one of the main cellular targets of GCNs. The mechanism of antitumor activity of GCNs is mainly dependent on disrupting the cellular redox balance and 2-OG homeostasis via inhibiting the activity of IDH1. 3. Natural products DY002 has a potent hypothermia-inducing and neuroprotective efficacy in animal models. we identify a novel hypothermia-inducing mechanism through the target identification of DY002.

Prof. Zhenhua LI

Professor
Affiliated Dongguan Hospital
Southern Medical University

Talk Title: **Biomimetic Materials for Hypoxic Tumor therapy**

Biography:

Dr. Zhenhua Li is the Professor of Southern Medical University. His research interests include the synthesis of biomimetic materials for cancer therapy and regenerative medicine.

Abstract:

Since Thomlinsons discovered the phenomenon of hypoxia in malignant tumors, it has been considered as one of the main reasons for the tolerance to radiotherapy and chemotherapy, and is also a potential cause of tumor recurrence and metastasis after treatment. In view of the important role of hypoxia in cancer disease progression and resistance to treatment, research on tumor hypoxia has attracted wide attention. At present, small molecule drugs based on tumor hypoxia have been used in clinic. However, there are still some problems in the use of small molecule drugs, such as poor solubility and short half-life of blood. With the advent of nanotechnology, more effective treatment strategies for hypoxic tumors have been rapidly developed.

Dr. Li has developed or utilized some biomimetic materials/living bacteria to deliver agents to enhance the efficacy of oxygen-dependent therapies by increasing tumor oxygen content. Utilizing the high porosity and excellent oxgen adsorption capacity of metal-organic framework (MOF) materials, ICG-based photodynamic therapy of hypoxia tumor was achieved. Subsequently, on the basis of this work, ZIF-67 was used as both a carrier of chemical drugs and a protector of CaO2 and DOX, Controlled release of Fenton-like reaction catalyst Co2+ and chemotherapeutic agent DOX was detected in responsive to tumor acidic microenvironments, Exposure of CaO2 to H2O increased the concentrations of O2 and H2O2 which was then converted to ROS in tumor tissue simultaneously for chemodynamic therapy. In addition, using cyanobacteria as oxygen production carriers, a complex of photosensitizer Ce6 and upconversion nanoparticles (UCNPs) was modified on the surface of cyanobacterial for enhanced photodynamic therapy of hypoxia tumor. The UCNPs was used as optical harvesting antenna system, which can convert high penetrating power 980 nm excitation light to visible light for the activation of Ce6 and cyanobacteria for in situ production of ROS. In addition, for the first time, we have discovered a kind of photosynthetic bacteria with hypoxic targeting, near-infrared phototaxis, and photothermal effect for hapoxia-targeting cancer therapy. Our self-infiltration of "living drugs" could accumulate into the hypoxic core of the tumor for efficient hypoxia tumor treatment without complicated post-modification.

Prof. Jin-Xin BEI

Professor
State Key Laboratory of Oncology in South China
Collaborative Innovation Center for Cancer Medicine
Cancer Center
Sun Yat-sen University

Talk Title: **Dissecting the Heterogeneity Nature of Ebv-Related Malignancies**

Biography:

Dr. BEI is a principal investigator and professor of molecular medicine at the State Key Laboratory of Oncology in South China, SYSUCC, the director of Core Facility of Biomedical Research, Center for Precision Medicine, Sun Yat-sen University (SYSU), China, and joint professor at the National Cancer Centre of Singapore. He obtained B.S. and PhD at SYSU and worked at Genome Institute of Singapore as Research Scientist before return to China. His major research interest is to dissect genetic and viral factors contributing to the development of cancers, as well as the underlying mechanisms. He has published around 100 scientific papers including those in prestigious journals such as Cell, Nat Genet, Lancet Oncol, etc. He has years of experience in organizing international collaborations. He was awarded Chang Jiang Scholar, Top-Notch Young Talents Program of China, and National Excellent Young Fellow, NSFC.

Abstract:

Remarkable prevalence of disease burden in Asia and Epstein-Barr Virus (EBV) infection are the two major features of EBV-related malignancies, such as nasopharyngeal carcinoma (NPC) and natural killer T cell lymphoma (NKTCL). Clinical presentations and survival outcomes are heterogenous among cancer patients. In this talk, different levels of intrinsic features would be discussed, which contribute to the various presentation and behaviour of EBV-related malignancies.

Session FIVE

Session Chair:

Prof. Xin CHEN &
Prof. Qi ZHAO

Session Title:

Tumor Immunology and Immunotherapy

Theme:

Immunity, Infection & Inflammation

24 July 2021

Prof. Youhai CHEN

Professor, Dean
Faculty of Pharmaceutical Sciences
CAS Shenzhen Institutes of Advanced Technology

Talk Title: **New Immune Checkpoints for Cancer therapy**

Biography:

Dr. Youhai Chen received his MB and MSc degrees from Shandong University in 1983 and 1986, respectively, and his PhD degree from the University of Manitoba, Canada, in 1993. After a postdoctoral training at Harvard Medical School, he joined the faculty of the University of Pennsylvania in 1995. He was a Professor of Pathology and Laboratory Medicine at Perelman School of Medicine, University of Pennsylvania, until 2020. In 2021, he became Chair Professor and Dean of Faculty of Pharmaceutical Sciences at Shenzhen Institute of Advanced Technology, Shenzhen, China. His research interests include immunity, inflammation and cancer. He has authored more than 150 research articles, and chaired a number of academic and administrative committees at academic or pharmaceutical institutions. He is a recipient of the Colyton Prize for Autoimmune Research.

Abstract:

Checkpoint inhibiting drugs targeting the PD1 pathway represent one of the most encouraging new therapeutics for cancer. Millions of cancer patients have benefited from using checkpoint inhibitors since their first approval in 2014 by the US FDA. However, most cancer patients do not respond to PD1 pathway inhibitors and those who do eventually develop disease progression. Therefore, there is a strong unmet need to improve the efficacy of PD1 pathway inhibitors or to develop drugs targeting new immune checkpoint regulators. In this talk, Dr. Chen will describe two classes of new immune checkpoint regulators called c-Rel and TIPE2. c-Rel is a member of the Rel/nuclear factor-kB (NF-kB) family, and a risk factor for human lymphoid cancers and inflammatory diseases. Using structure-based drug discovery and medicinal chemistry approaches, Dr. Chen's group has developed a new class of small molecules that inhibits c-Rel function by preventing its binding to DNA. As expected, these compounds are highly effective in blocking tumor growth in mice. Upon co-administration into mice, the c-Rel blockers significantly enhance the anti-tumor activity of the PD1 inhibiting drugs. They are in the process of (i) defining the mechanisms through which c-Rel controls tumor growth, (ii) establishing the efficacy of their c-Rel inhibitors for the treatment of common cancers, and (iii) performing IND-enabling studies.

Prof. Zhe-Xiong LIAN

Professor
School of Medicine
South China University of Technology

Talk Title: **Hepatic Cd8+ T Cells In Autoimmune Liver Diseases**

Biography:

Professor Zhe-Xiong Lian is mainly engaged in the basic immunological research of autoimmune liver disease. and made outstanding contributions to the research of primary biliary cholangitis (PBC). He was involved in the discovery of PBC-specific CD8+ T cells and the development of a variety of transgenic mouse models capable of mimicating bile duct-specific immune injury, serological characteristics, and chronic development in human PBC. Use of these mice models and clinical samples, Prof. Lian devoted himself to explore the factors of immune cells, cytokines, and chemokine receptors on the pathogenesis of PBC process and the role of hematopoietic system abnormality for the decade years, greatly promoted the PBC basic and clinical research, revealed the immune pathological mechanism of autoimmune liver disease and new clinical immunotherapy. Prof. Lian has published more than 140 papers in high quality scientific journals and got high international reputation in the field of autoimmune liver disease.

Abstract:

Autoimmune liver diseases (ALD) are characterized by the destruction of the liver parenchyma and/or the hepatic bile ducts mediated by autoreactive T cells. The function and mechanism of CD8+ T cells in autoimmune liver diseases still remain elusive. We confirmed the expanded hepatic CD8+ T cells in our ALD model mice exhibited high functional activation rather than exhaustion which producing high levels of IFN-γ and granzyme-B, and showed obvious higher cytotoxic activity. These data indicate that chronic antigen stimulation induced by the breach of immune tolerance drives the induction and expansion of autoreactive hepatic CD8+ T cells, which showed high cytotoxicity to hepatocytes and induced the liver injury. These findings provide potential targeting strategies for the therapeutic application of autoimmune liver diseases

Prof. Fubin LI

Principal Investigator
School of Medicine
Shanghai Institute of Immunology
Shanghai Jiao Tong University

Talk Title: **Progress in Understanding Antibody Agonism – An Unnatural Mode of Action**

Biography:

Dr. Fubin Li is a principal investigator at Shanghai Institute of Immunology, Shanghai Jiao Tong University School of Medicine. His research focuses on the following two directions: 1) to understand how different antibody functions, such as agonistic and pathogenic function, are regulated by antibody intrinsic and extrinsic factors, and to develop novel methods to modulate antibody activity based on the understanding of fundamental principles, including strategies for optimizing agnostic cancer immunotherapeutic antibodies; 2) to understand how protective and autoreactive B cell differentiation is regulated. He has published more than 20 original papers in Science, Journal of Experimental of Medicine，PNAS, Nature Communications, Journal of Immunology et al. He has also applied for four patent applications (two licensed). His research is supported by NSFC key grant and Fund for Excellent Young Scholars.

Abstract:

The agonistic antibody has been extensively studied in animal models and is widely considered a promising therapy class for treating cancer and other diseases. Yet, not a single immune agonistic antibody has been approved after nearly 20 years of clinical testing. The challenge in agonistic antibody development and progress will be reviewed, and the progress in understanding antibody agonism will be discussed.

Prof. Fan PAN

Chair-Professor, Co-Director
Center for Cancer Immunology
Shenzhen Institutes of Advanced Technology
Chinese Academy of Sciences

Talk Title: **Targeting Regulatory T cells in Tumor Immunotherapy**

Biography:

Dr. Fan Pan is a Chair-Professor of Cancer Immunology and Co-Director of Center for Cancer Immunology, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences. Before this position, he was the Vice President & CSO of NanoBiotec Inc, NJ and an Associate Professor of Oncology Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Johns Hopkins University School of Medicine. He received his MD in Shanxi Medical University, MS in Shanxi Medical University (Preventive Medicine) and PhD in Chinese Academy of Preventive Medicine (Immunology). His overall research interests concern the molecule mechanisms controlling the development, lineage stability and function of T cell subsets. Moreover, he focuses on Treg and effector T cells, which are important for immune control and immune activation, respectively. He also focuses on the interplay of metabolism and immunity, pathways of posttranslational Foxp3 regulation, as well as the coregulator molecules facilitating this key Treg transcription factor's function and Treg-mediated immune control. Through these discoveries, he aims to develop novel immunotherapy or manipulating immune system to treat cancer and other immune-related diseases.

Abstract:

Regulatory T (Treg) cells suppress abnormal/excessive immune responses to self- and nonself-antigens to maintain immune homeostasis. In tumor immunity, Treg cells are involved in tumor development and progression by inhibiting antitumor immunity. Infiltration of Treg cells into the tumor microenvironment (TME) occurs in multiple murine and human tumors. A high Treg infiltration is associated with poor survival in various types of cancer. Therefore, strategies to deplete Treg cells and control of Treg cell functions to increase anti-tumor immune responses are urgently required in the cancer immunotherapy field. Recently, our lab has demonstrated that YAP is essential for Treg-mediated suppression of antitumor immunity (Cancer Discovery, 2018). Furthermore, our lab also unrevealed that Traf6 is a critical E3 ligase for Foxp3-meiated regulatory T-cell function through K63-linked ubiquitination (EMBO J, 2019). By pursuing these research avenues we wish to develop novel therapeutic strategies to enhance anti-tumor immunity.

Prof. Zhiwei CHEN

DVM Director, AIDS Institute Professor
Department of Microbiology
LKS Faculty of Medicine
The University of Hong Kong DVM

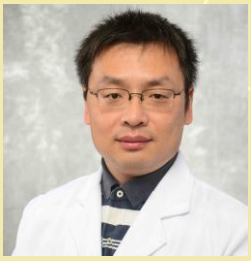
Talk Title: **Isoformic Regulation of Exhausted T Cells in Hepatocellular Carcinoma**

Biography:

Prof. Zhiwei Chen is the director of AIDS Institute and a tenured professor in Microbiology at University of Hong Kong. He obtained his PhD from New York University in 1996. He then progressed from a post-doc to a research scientist, and to a staff investigator/assistant professor at the Aaron Diamond AIDS Research Center of the Rockefeller University. Since 1991, he has been studying HIV/AIDS. In recent years, he also investigates COVID-19 vaccine and immunopathogenesis as well as cancer immunotherapy. He has published over a hundred thirty peer-reviewed SCI papers. He serves the editorial boards of AIDS, JAIDS, JMP and JNIP.

Abstract:

Checkpoint inhibitor immunotherapy has significantly improved current cancer treatment, yet the mechanism underlying resistance to PD-1 blockade in patients with hepatocellular carcinoma (HCC) remains elusive. In this study, we analyzed a cohort of 38 HCC patients using freshly isolated peripheral blood mononuclear cell (PBMC), 25 samples of parried HCC and adjacent non-tumor tissues, as well as 6 HCC patients treated with Nivolumab. We demonstrated that HCC-induced PD-1 isoform as a possible mechanism conferring resistance to PD-1 blockade and warranted the development of an isoform-specific antibody for cancer immunotherapy.



Prof. Han LIU

Principal Investigator
Ruijin Hospital
Shanghai Jiao Tong University School of Medicine

Talk Title: **A T-Cell Independent Universal Cellular therapy Strategy**

Biography:

Dr. Han Liu received his BS degree in Biotechnology and MS degree in Biochemistry and Molecular Biology in Peking University, He further received his PhD degree in Genetics in School of Medicine, Shanghai Jiao Tong University. He the undergo his postdoctoral training in Shanghai Institute of Hematology, Shanghai Jiao Tong University School of Medicine / Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, China and Division of Oncology, Washington University in St. Louis School of Medicine, St. Louis, MO. Then he became a Research Instructor in the Division of Oncology, Washington University in St. Louis School of Medicine, St. Louis, MO and Senior Research Scientist in the Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, New York, NY. He received several awards such as Shanghai Academic Research Leader, Principal Investigator of National Key Research and Development Program of China, Shanghai Shu Guang Scholar, American Society of Hematology (ASH) Scholar Award, etc. He is also the committee member of the Experimental Hematology Section of Chinese Association of Pathophysiology and the council member of the Cell Therapy Research and Application Branch of Chinese Society for Cell Biology.

Abstract:

To be provided.

Session SIX

Session Chair:

Prof. Wenhua ZHENG

Session Title:

Neuroscience, Aging and Degenerative Diseases

24 July 2021

Prof. Wenhua ZHENG

Professor
Faculty of Health Sciences
University of Macau

Talk Title:

Neuronaprotective Effect of Artemisinin and Its Derivatives (Arts) and Their Implication in the Treatment of Alzheimer's Disease

Biography:

Dr. Wenhua Zheng, Professor, Principle Investigator in the Faculty of Health Sciences, University of Macau, leads a group of scientists to study new therapeutic targets involved in aging and in several degenerative disorders like Alzeimer's Disease; new functions and downstream targets of PI3k/ Akt /FoxO transcriptional factors; the neuroprotective effect of Artemisinin and the development of new drugs. Prof Zheng is the Vice Chairman of 3th Board of Specialty Committee of World Federation of Chinese Medicine Societies; Standing Committee Member of the Epigenetic Professional Committee of the Chinese Pharmacological Society (CPS), a Section Editor for Encyclopedia of Gerontology and Population Aging; a Lead Guest Editor and Editor. He is an Adjunct Professor at RMIT University and an Honorary Professor at the University of Queensland (QS45) in Australia. Prof Zheng has published >150 papers in journals such as JBC, Free Radical of Biology and Medicine, and Radox Biology. These papers have been cited over 5500 times.

Abstract:

Alzheimer's Disease (AD), characterized by the progressive loss of cognitive function, is the most common neurodegenerative disorder. It is marked by the occurrence of neuronal loss, the accumulation of β-amyloid (Aβ) plaques and neurofibrillary tangles. AD etiology is still unknown, and currently there is no effective treatment to cure or prevent it. Artemisinin and its derivatives are safe and effective antimalarials, which have been used for decades in the clinic saving millions of lives. We have recently discovered that, artemisinin has a neuroprotective effect. Since it is affordable, safe and able to cross the blood-brain barrier, this discovery offers new promising therapeutic indications for artemisinin in diseases of the central nervous system. We have found that artemisinin/artemether promoted the survival of several neuronal cells. In fact, pretreatment of PC12 cells with artemisinin/artemether significantly inhibited Aβ1-42-induced cell death, reduced intracellular reactive oxygen species (ROS) production, prevented mitochondrial membrane potential loss and reduced LDH release and caspase 3/7 activation. Western blot analysis revealed that artemisinin/artemether stimulated the phosphorylation/activation of ERK, AMPK and CREB while inhibition of the ERK/AMPK signaling pathways, by either ERK pathway inhibitor PD98059/AMPK inhibitor Compound C, reduced the expression of ERK/AMPK with siRNA blocking the protective effect of artemisinin/artemether. Similar results were obtained in other neuronal cells and primary cultured neurons. These findings suggest that artemisinin/artemether is a potential neuroprotective agent that inhibits various toxin-induced cell death by activating signaling pathways such as ERK/AMPK/autophagy. In addition, artemisinin/artemether significantly improved the cognitive impairment and reversed several pathological changes in AD mice. It reduced neuronal cell death, Aβ deposit and tau phosphorylation, increased neuronal regeneration and cholinergic function, inhibited the inflammatory response and over-activation of glial cells. These results demonstrate that artemisinin and its derivatives can improve various symptoms and pathological changes of AD through neuroprotection, reducing amyloidogenesis/tau hyperphosphorylation and inflammation, functioning as a new multi-target neuroprotective/anti-AD agent. These findings support the potential application of artemisinin and its derivatives on the prevention and treatment of neurodegenerative diseases such as AD.

Prof. Jian-Hui LIANG

Professor
School of Pharmaceutical Sciences
Department of Molecular and Cellular Pharmacology
Peking University

Talk Title: **Role of Molecular Chaperone Hsp70 in Morphine Addiction**

Biography:

Jian-Hui Liang studied in the department of clinical medicine, Hengyang College of Medicine, University of South China and obtained the bachelor of clinical medicine, from September 1978 to July 1983. And then he held the post of psychiatrist-in-residency and psychiatrist-in-charge (License No. 19991111) in the Mental Hospital of Chenzhou Prefecture. Hunan, China (September 1983 to August 1990). He carried out his MD/PhD in social psychiatry, the Institute of Mental Health of Peking University, Beijing, China, investigating and surveying the course and outcome of schizophrenia in the rural community of Beijing western suburb for 5 years (September 1990 to July 1995). From September 1995 to February 1998, he worked as a postdoctoral to research and develop some new antidepressants in Beijing Institute of Toxicology and Pharmacology. He gained an associate professorship in Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical University, in 1999 and a full professorship in the Centre of Health Sciences, Peking University, in 2004. He was a visiting fellow in Institute of Natural Medicine, University of Toyama, Japan, in 1998 and a visiting scientist in Howard Florey Institute, University of Melbourne, Australia, in 2004. He presided over the revision of China's Catalogue of Narcotic drugs (2013 edition) and China's Catalogue of Psychotropic drugs (2013 edition). He specialises in understanding "chaperone-mediated opioid addiction" and has developed Liang's contextual-stress box to induce depression- and/or anxiety-like behaviour in mice. He serves as deputy chief editor on "Metabolic Brain Disease" (2015-) and as reviewing editor on "Pharmacology Research & Perspectives", and plays an active role in Chinese society of neuropsychopharmacology.

Abstract:

Rationale: Hsp70 serves as a powerful chaperone required for the activation and stabilization of proteins, mediating fundamental cellular processes. This study aimed to study the involvement of Hsp70 in morphine-induced behavioral sensitization closely related to drug addiction. Methods: Behavioral sensitization to morphine was induced by the single-dose paradigm in mice and rats. An RT-PCR array and Western blot were used to test changes in Hsp70 gene and protein expression in Nucleus Accumbens (NAc) of mice and rats. Further, we observed effects of transcription (actinomycin D), protein synthesis (cycloheximide), Hsp70 inhibitors (KNK437, methylene blue, and pifithrin-μ) or inducer (geranylgeranylacetone) on Hsp70 expression and behavioral sensitization. Results: 1 Behavioral sensitization was evident in mice and rats pretreated with a single morphine injection; 2 The increased expression of Hsp70 gene and protein in NAc of mice and rats was parallel to behavioral sensitization; 3 Transcription and protein synthesis inhibitors could not only block behavioral sensitization, but also decrease Hsp70 expression; 4 Hsp70 inhibitors attenuated behavioral sensitization, while inducer promoted it. Conclusion: Hsp70 as a chaperone is critically involved in behavioral sensitization to morphine and the theory of "Chaperone-mediated opioid addiction" is hypothesized.

Prof. Jiangping XU

Professor, Chair of Pharmacology
Southern Medical University

Talk Title: Regulatory Mechanism of Phosphodiestase 4-Mediated Signal Pathways in Parkinson's Disease

Biography:

Dr. Xu is the Doctor of pharmacology, professor of Southern Medical University (second post), academic leader of the neurological and metabolic disease drug research innovation group of the School of Pharmacy; new drug review expert of the National and Guangdong Food and Drug Administration. In recent years, he has mainly engaged in basic neuropsychopharmacology and preclinical evaluation of new drugs, focusing on the research and development of drugs for psychiatric diseases such as elderly neurodegenerative diseases and depression.

Abstract:

Parkinson's disease (PD) is a neurodegenerative disease caused by dopaminergic neuronal lesions in the substantia nigra pars compacta (SNpc) and striatum. we explored the roles and mechanisms of PDE4 in the neurodegeneration of dopaminergic neurons based on the *in vivo* and *in vitro* model of PD. The results show that Inhibition of PDE4 had anti-apoptotic effects on model cells induced by MPP+ or overexpressed α-synucleinA53T mutants, improved the motor deficiency of MPTP model mice, and played a neuroprotective role on dopaminergic neurons by activating the cAMP/EPAC/Akt signaling pathway, CREB/PGC-1α signaling pathway and AMPK-dependent autophagy pathway.

Prof. Ligang CHEN

Professor, Director of Neurosurgery, Director of General Surgery
The Affiliated Hospital of Southwest Medical University

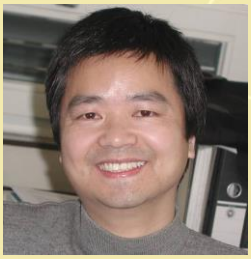
Talk Title: **Deep Brain Stimulation Robot-Assisted Surgery for Parkinson'S Disease**

Biography:

Dr. Chen is the Professor, PhD, doctoral supervisor, State Council Special Allowance Expert, National Natural Science Foundation Review Expert, Sichuan Province Academic and Technical Leader, Director of the Department of Surgery, Director of General Surgery, Director of Neurosurgery, Director of PI Laboratory, Affiliated Hospital of Southwest Medical University and Director of Sichuan Neurosurgery Clinical Research Center.

Abstract:

To retrospectively analyze robot-assisted deep brain stimulation (DBS) surgery for Parkinson's Disease (PD)relevant studies from 2015 to 2021. The results demonstrated that the duration of the procedure was significantly shorter in the robot-assisted group than in the traditional stereotactic surgery group.Moreover,the stimulation parameters, electrode implantation accuracy, intracranial air, intraoperative electrophysiological signal length, complications, and Unified PD Rating Scale (UPDRS) measurements have no significant difference between two groups. Robot-assisted asleep DBS surgery is a promising surgical method for PD.



Prof. Zhongshu TANG

Professor
Zhongshan Ophthalmic Center
Sun Yat-sen University

Talk Title: **Mechanism of Amblyopia**

Biography:

Dr. Tang received his Master degree in Neuroscience from the former Institute of Physiology, Chinese Academy of Sciences, and his PhD training in Neurochemistry Dept. Max-Planck-Institute for Brain Research. He subsequently joined NEI/NIH for his postdoctoral training. In 2012, he joined the State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University. His academic background covers: 1. Functions of the VEGF/PDGF families in angiogenesis and neuroprotection. 2.Stem cell therapy of Parkinson's disease. 3. Functions and mechanisms of sumoylation. In the last years, Dr. Tang is involved in the mechanim study and therapy trial of glaucoma and amblyopia.

Abstract:

Amblyopia is an eye disease that leads to monocular visual acuity loss, and in some cases, biocular visual acuity loss. The most common causes for amblyopia are strabismus, anisometropia, ametropia and deprivation. Bilateral amblyopia can be caused by bilateral cataract, bilateral high refractive error, or bilateral ptosis. Occlusion therapy is a traditiaonal and successful treatment for amblyopia. Pharmacological treatments, such as the combination of levodopa and carbidopa, are also in trials. Despite the fact that we have known about amblyopia for over 200 years, and the clinical treatment is basically sucsessful, the mechnism underlying is still largely unknown. This embarrassed situation not only limits us to explore more streatments, but also compromises the effects of current treatments.

We know that amblyopia is a developmental visual system disease, and we believe that problems are located in the brain, but we do not know exactly what and where they are. To investigate the molecular mechanism of amblyopia, we created a primate monocular deprived amblyopia model. Visual system tissues in the brain were isolated for RNA sequencing. From the mRNA sequencing data of LGN, we got 818 differentially expressed genes. After GO and KEGG enrichment, we obtained significant enrichment pathways such as neural development and synaptogenesis. We selected a couple of receptors for verification. DRD1 (Dopamine Receptor D1) is one of them. After verification by QPCR with monkey and mouse amblyopia samples, we performed immunofluorescence staining in mouse brain sections. In the dLGN to which RGCs project directly, the expression of DRD1 in the monocular deprived amblyopia group was much lower than that in the control group.

Conclusion: DRD1 expresses decreases dramatically in monocular deprived amblyopia model. This finding explain the outcome of levodopa treatment. It may be one reason for the formation of amblyopia and may be a new target for the treatment of amblyopia.

Prof. Aihua LIU

Professor, Chief Physician
Beijing Tiantan Hospital
Capital Medical University

Talk Title: Exosome-Encapsulated Microrna-140-5P Alleviates Neuronal Injury Following Subarachnoid Hemorrhage By Regulating Igfbp5-Mediated Pi3K/Akt Signaling Pathway

Biography:

Dr. Aihua Liu is the Professor, doctoral supervisor and Chief physician of the Department of Interventional Neuroradiology, Beijing Neurosurgical Institute, Beijing Tiantan Hospital, Capital Medical University,

Abstract:

Background: Exosomes secreted by adipose tissue-derived stromal cells (ADSCs) have shown therapeutic effects in regenerative medicine. Here, we examined the effects of exosome-encapsulated microRNA--140-5p (miR-140-5p) on neuronal injury following subarachnoid hemorrhage (SAH).

Methods: Primary neurons and ADSCs were isolated. Neurons were cultured with ADSCs-derived exosomes (ADSC-Exos). TDP-43 aggregated neurons were established and treated with PKH67-ADSC-Exos and Cy3-miR-140-5p to assess if ADSC-Exos could deliver miR-140-5p into the neurons. Viability and apoptosis of TDP-43 aggregated neurons were assessed in a co-culture system with ADSC-Exos. The putative interaction between miR-140-5p and IGFBP5 was analyzed using luciferase assay. Gain-of-function approach was used to analyze if IGFBP5 was involved in mediating neuronal injury. The role of PI3K/AKT signaling pathway in mediating neuronal injury was analyzed using treatment with Miltefosine (inhibitor of PI3K/AKT signaling pathway). Thereafter, SAH rat models were established to confirm the *in vitro* findings.

Results: ADSC-Exos inhibited TDP-43 aggregation-induced injury to neurons by enhancing viability but suppressing apoptosis. miR-140-5p could be transferred from ADSC-Exos to neurons to down-regulate IGFBP5 expression. Besides, miR-140-5p delivered by ADSC-Exos prevented TDP-43 aggregation-induced injury by suppressing IGFBP5 through activation of the PI3K/AKT signaling pathway. Furthermore, *in vivo* findings also confirmed the protective role of ADSCs-derived exosomal miR-140-5p against SAH-induced neurological impairment. Conclusions: Our study uncovered the inhibitory role of ADSCs-derived exosomal miR-140-5p on neuronal injury following SAH through down-regulation of IGFBP5.

Session SEVEN

Session Chair:

Prof. Shaoping LI &
Prof. Simon LEE

Session Title:

Traditional Medicines and Drug Discovery

24 July 2021

Prof. Jinsong BIAN

Professor; Chair
Department of Pharmacology
Department of PharmacH56 Medicine
Southern University of Science and Technology

Talk Title: **Targeting Na+/K+ Atpase to Treat Parkinson'S Disease**

Biography:

Dr. Jinsong Bian is a full Professor and head of Department of Pharmacology, School of Medicine, Southern University of Science and Technology, Shenzhen, China. He earned his PhD degree from the University of Hong Kong and was awarded the Dr KP Stephen Chang Gold Medal for outstanding performance in the degree of Doctor of Philosophy in 2000. His main research interests include 1. Pathophysiology of pulmonary hypertension; 2. Novel functions of Na+/K+ ATPase; 3. Biology of endogenous mediators. He has published over 130 papers in international journals including Science Advances, Cir Res, Pharm Therap, Redox Biology, JASN, and has delivered over 80 lectures at the invitation of international and regional scientific societies, institutes and conference organizers. His Google scholar Citations is ~10,000 and H-index is 51.

Abstract:

Na+/K+-ATPase (NKA) plays important roles in maintaining cellular homeostasis. Reduced NKA activity has been reported in aging and neurodegenerative diseases. However, little is known about the function of NKA in the pathogenesis of Parkinson's disease (PD). Here, we report that reduction of NKA activity aggravates α-Synuclein-induced pathology and deficits in behavioral tests for memory, learning, and motor function. We generated an NKA-stabilizing monoclonal antibody, DR5-12D, against the DR region of the NKAα1 subunit. We demonstrate that DR5-12D can ameliorate α-synuclein-induced TH loss and behavioral deficits by accelerating α-synuclein degradation in neurons. The underlying mechanism for the beneficial effects of DR5-12D involves activation of NKAα1-dependent autophagy via increased AMPK/mTOR/ULK1 pathway signaling. Cumulatively, this work demonstrates that NKA activity is neuroprotective and that pharmacological activation of this pathway represents a new therapeutic strategy

Prof. Maggie Pui-Man HOI

Associate Professor
Institute of Chinese Medical Sciences
University of Macau

Talk Title: Discovery and Development of New Drug From Chinese Medicines Against Cerebrovascular and Neurodegenerative Diseases

Biography:

Dr. Maggie Hoi was born and raised in Macau and finished her high school education in Macau. She then furthered her education in the United Kingdom. She studied her Bachelor of Science in Pharmacology at University College London and her PhD at University of Cambridge in Cardiovascular Pharmacology. Upon graduation, she returned back to Macau and started to embark her research career in the Institute of Chinese Medical Sciences (ICMS) at the University of Macau since 2007 and has been faculty member since 2010. Her current research interests include drug discovery from Chinese herbal medicine for treating cardiovascular and cerebrovascular diseases, and strategies for prevention of these diseases by investigating the molecular, cellular and physiological mechanisms of drug actions. Since joining the University of Macau, she has published more than 40 articles in international peer-reviewed scientific journals and has served at principle investigator of more than 8 scientific projects in the area of pharmacology and herbal medicine.

Abstract:

Cerebrovascular and neurodegenerative diseases are tightly associated with each others and are increasing harmful to our health and life. The global disease projection indicates that the healthcare burden derived from these disease problems will continue to rise. Many traditional Chinese medicines (CMs) have also been used to prevent and treat the multi-faceted diseases in China and other Asian countries. These herbs are potential rich sources of new leads that may also reveal previously unidentified mechanisms. Previously, our team has initiated a research program to analyze and characterize the bioactive extracts and pure natural components from the CMs using multiple experimental models of cerebrovascular and neurodegenerative diseases. Also, some of the natural bioactive compounds have been further chemically modified to series of derivatives using different organic chemistry approaches and proven improved potency. Our drug screen results provide scientific rationales for clinical usage of the CMs and also probably lead to develop reproducible, higher potency and lower toxic agents for healthcare in the future.

Prof. Li FU

Professor

Jilin University & Dalian Fusheng Natural Medicine Research Institute

Talk Title: **Discovery and Development of Single Compound Chinese Medicine Ginsenoside Rg3**

Biography:

Dr. Li Fu is the dean of Dalian Fusheng Natural Medicine Research Institute, and also an adjunct professor and doctoral supervisor at School of Pharmaceutical Sciences, Jilin University. She has accumulated experiences of research and development focusing on innovative R&D and industrialization of single compound new Chinese medicine and international botanical drugs. As the primary investigator, she won the second prize of the State Technological Invention Award.

Abstract:

The discovery and systematic studies of single compound Chinese medicine ginsenoside Rg3 were introduced in this topic, including non-clinical pharmaceutics, pharmacodynamics, toxicology, pharmacokinetics, the mechanism study of anti-tumor metastasis, and clinical studies of phase I, phase II-III, and phase IV and post-marketing re-evaluation, as well as future focus of ginsenoside Rg3 new drugs development for discussion. In addition, author's experience and insights of innovative drugs development were expounded through diverse paths of new drug discovery, druggability and protection of core technologies.

Prof. Ailin LIU

Professor
Institute of Materia Medica
Chinese Academy of Medical Sciences & Peking Union Medical College

Talk Title: **Discovery of Drug Candidates Towards Sars-Cov-2 Via Targeting Virus-Host Interactome**

Biography:

Dr. Ailin Liu is the Professor of the Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College.

Abstract:

Coronavirus disease-2019 (COVID-19) is currently still growing throughout the globe, causing a serious health threat. Although some therapeutic agents have showed potential prevention or treatment, there is no specific drug discovered for this pandemic. Hence, it is urgently needed to identify the promising therapeutic agents against COVID-19. Targeting virus-host interactome provides a more effective strategy for antivirus drug discovery compared with targeting virus proteins. In this study, we proposed a network-based framework to identify the potential drug candidates against COVID-19 from approved drugs and natural products via targeting host proteins of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). We firstly meatured the network distances between drug targets and COVID-19 disease modules using network proximity approach, and identified that 229 approved drugs as well as 432 natural products had significant associations with SARS-CoV-2. After searching for literature evidence of drug candidates, we found that 60.7% (139/229) of approved drugs and 39.8% (172/432) of natural products with reported antiviral and antiinflammatory evidence. We further integrated our network-based predictions and validated their anti-SARS-CoV-2 activities by experimental assays. Four drug candidates, including hesperidin, isorhapontigenin, salmeterol and gallocatechin-7-gallate, have exhibited anti- SARS-CoV-2 effect on SARS-COV-2 virus infected Vero cells. Finally, we showcased the mechanism of actions of two drug candidates (isorhapontigenin and salmeterol) on COVID-19 via network analysis. Overall, this study offers forceful approaches for in silico identification of drug candidates on COVID-19, which will facilitate the discovery of antiviral therapeutics against SARS-CoV-2.

Prof. Wen-Cai YE

Professor, Vice Rector
College of Pharmacy
Jinan University

Talk Title: Bioactive Constituents and Innovative Drugs Research From the Traditional Chinese Medicine and Natural Products

Biography:

Wen-Cai Ye is a professor at Jinan University (in Guangzhou of China), Changjiang Scholar Distinguished Professor, the winner of the National Natural Science Foundation for Distinguished Young Scholars award and the National Innovation Competition Award. He began his research career in Pharmacy at the China Pharmaceutical University, where he received his bachelor degree in 1983. He received his PhD in Chemistry in 2001 at the Hong Kong University of Science & Technology. In 2002, he joined the College of Pharmacy at Jinan University. The research topics of Professor Ye focus on natural bioactive molecules and their mechanism of action. He has found more than 1600 new compounds from TCM and herbal medicines, including more than 50 bioactive constituents with potent anticancer, antiviral, and neuroprotective activities. Professor Ye is (co)author of over 500 peer-reviewed papers including published in the journals of JACS, J. Clin. Invest., Mol. Psychiatry, Hepatology, Angew. Chem. Int. Ed., etc, and inventor of 49 licensed patents.

Abstract:

In the history of human drug discovery, some important drugs, such as morphine, penicillin, aspirin, paclitaxel, artemisinin, etc. come from natural products or their derivatives. The research on innovative drugs derived from traditional Chinese medicine and natural products is an effective way suitable for China's national conditions.

In recent years, our group had carried out systematically chemical and biological investigations on the medicinal plants in China and South American. More than 150 medicinal plants, such as the plants from genus Flueggea, and families Apocynaceae and Myrtaceae, were involved in our research. As a result, more than 6500 compounds, mainly Securinega alkaloids, phloroglucinol derivatives and monomeric indole alkaloids, were isolated, including 1600 novel compounds with more than 130 unprecedented skeletons. Twenty of them were reported as Hot off the press by Nat Pord Rep. A library of natural products and their derivatives with various structural types was established, including more than 8000 natural compounds and components. More than 20 lead compounds with anti-tumor, antiviral, antibacterial and neuroprotective activities were discovered from the natural products library, and several new drug candidates were also obtained.