香港浸會大學
HONG KONG BAPTIST UNIVERSITY

School of 中醫藥學院
Chinese Medicine

Mr. and Mrs. Ko Chi Ming Centre for Parkinson's Disease Research (CPDR)
Hong Kong Baptist University

GMCNS 金衛醫療神經再生研究中心
Golden Meditech Centre for NeuroRegeneration Sciences

2025 SYMPOSIUM ON

AUTOPHAGY, AGING, CANCER AND NEURODEGENERATION : THERAPEUTIC POTENTIAL OF CHINESE MEDICINE

28 JULY 2025 (MON)

09:10 AM TO 12:50 PM

➢ VENUE

TIN KA PING GLOBAL CONFERENCE ROOM, UG06
JOCKEY CLUB CAMPUS OF CREATIVITY, HKBU

PROGRAMME

09:00 – 09:10 **Reception & Registration**

09:10 – 09:20 **Opening Remarks**

- ***Welcoming Address***
  Professor Min Li
  Dean, School of Chinese Medicine, Hong Kong Baptist University
- ***Group Photo***

Session 1: Aging and Cancer – Mechanisms and Therapeutic Targets

Moderator: Professor King-ho Cheung
Professor, School of Chinese Medicine, Hong Kong Baptist University

09:20 – 09:50 **C/EBPβ/AEP Signaling: A Universal Aging Driver?**
Professor Keqiang Ye
Endowed Professor and Dean, Department of Biology,
Faculty of Life & Health Sciences, Shenzhen University of Advanced Technology

09:50 – 10:20 **Nitrogen Metabolism in Liver Cancer**
Professor Wei-Xing Zong
Distinguished Professor and Department Chair, John L. Colaizzi Endowed Professor,
Department of Chemical Biology, Ernest Mario School of Pharmacy,
Rutgers University, U.S.A.

10:20 – 10:40 **Coffee Break**

Session 2: Autophagy – Mechanisms and Novel Regulators

Moderator: Dr. Ashok Iyaswamy
Research Assistant Professor, School of Chinese Medicine, Hong Kong Baptist University

10:40 – 11:10 **Novel Regulatory Mechanisms of Mitophagy: From Transcription to Post-translational Modifications of PINK1**
Professor Hanming Shen
Chair Professor, Associate Dean (Teaching), Faculty of Health Sciences,
University of Macau

11:10 – 11:40 **The Beclin 1-Vps34 Molecular Machinery in the Autophagy Process: Structural Studies and Design of Novel Modulators**
Professor Yanxiang Zhao
Professor, Department of Applied Biology and Chemical Technology,
The Hong Kong Polytechnic University

Session 3: Autophagy Modulation by TCM in Neurodegeneration

Moderator: Dr. Zhiqiang Deng
Research Assistant Professor, School of Chinese Medicine, Hong Kong Baptist University

11:40 – 12:10 **Artificial Intelligence-assisted Discovery of Neuroprotective Autophagy Enhancers**
Professor Jiahong Lu
Associate Professor, Deputy Director (Research and Technology Transfer),
Institute of Chinese Medical Sciences, University of Macau

12:10 – 12:40 **Acupuncture Alleviates Alzheimer's Pathology by Modulating Autophagy and Cellular Senescence**
Professor Juxian Song
Professor, School of Pharmacy, Chengdu University of Traditional Chinese Medicine

12:40 – 12:50 **Closing Remarks**

Each 25-minute lecture is followed by a 5-minute Q&A.

Biographies & Abstracts of Speakers

Professor Keqiang Ye

Endowed Professor and Dean,
Department of Biology,
Faculty of Life & Health Sciences,
Shenzhen University of Advanced Technology

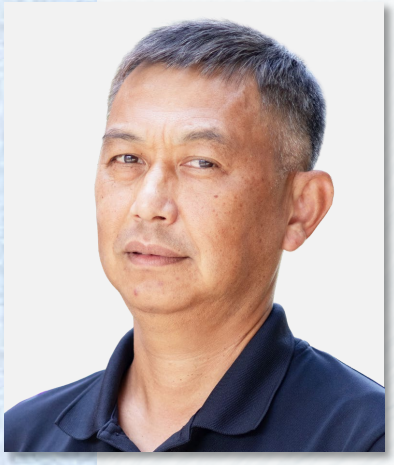
BIOGRAPHY

Professor Keqiang Ye is a distinguished researcher in the fields of neurology and neuroscience, currently serving as Endowed Professor and Dean at the Department of Biology, Faculty of Life & Health Sciences at Shenzhen University of Advanced Technology in China. He has an impressive publication record, with articles featured in renowned journals such as Nature, PNAS, and the Journal of Alzheimer's Disease. Professor Ye's research primarily focuses on the molecular mechanisms underlying neurodegenerative diseases, including Alzheimer's and Parkinson's diseases. He is recognized as a leading figure in the study of autophagy and its implications for neurodegeneration, having identified several key regulators and pathways that influence disease progression. His work has significantly advanced our understanding of potential therapeutic targets for neurodegenerative disorders. Professor Ye has received numerous awards for his contributions to the field and plays a vital role in both basic and translational research aimed at combating neurodegenerative diseases.

C/EBPβ/AEP Signaling: A Universal Aging Driver?

ABSTRACT

Mammalian AEP is a cysteine protease that cleaves its substrates after asparagine residues. In humans, AEP is encoded by the *LGMN* gene. AEP levels are escalated in the brain in an age-dependent manner, cleaving APP and Tau at N585 and N368, respectively, and triggering Ab amyloids and Tau aggregation. Knockout of AEP substantially ameliorates AD (Alzheimer's disease) pathologies in AD mouse models, restoring the behavioral functions. Inhibition of AEP by small molecules robustly reduces AD pathologies, attenuating the behavioral deficits. C/EBPb acts as a major transcription factor for *LGMN*, and neuronal C/EBPb transgenic mice (Thy1-C/EBPb Tg; Tg/Tg) display gene dose-dependent short lifespan. Deletion of AEP from Thy1-C/EBPb Tg mice extends the lifespan. The longevity phenomena also apply to *c. elegans*. Inhibition of AEP with its inhibitor elongates the worm and mice lifespan. Notably, C/EBPb/AEP signaling progressively escalates and peaks in human brains from 70-80s, and starts decline after 90s, inversely correlated with insulin signaling in the brain. Strikingly, overexpression of C/EBPb plant homologs ABFs or GBFs facilitates the senescence, whereas deletion of these genes delays the aging. The same scenarios are also found to VPEs, homologues of plant *LGMN*. Thus, blockade of AEP with its inhibitors may provide an innovative strategy for elongating the lifespan.



Professor Wei-Xing Zong

Distinguished Professor and Department Chair, John L. Colaizzi Endowed Professor,
Department of Chemical Biology,
Ernest Mario School of Pharmacy,
Rutgers University, U.S.A.

BIOGRAPHY

Professor Wei-Xing Zong is a world-renowned cancer researcher. He currently serves as the John L. Colaizzi Endowed Chair and Distinguished Professor at the Ernest Mario School of Pharmacy, Rutgers University. He holds a Ph.D. from the University of Medicine and Dentistry of New Jersey and has completed postdoctoral training at the University of Pennsylvania. Professor Zong's research focuses on cell metabolism and protein homeostasis in oncogenesis and cancer treatment, utilizing advanced molecular and biochemical techniques to study apoptosis, autophagy, and metabolic processes. With over 110 peer-reviewed papers and 39,000 citations, his work has been published in high-impact journals such as Science, Nature, and Cell. He has been continuously funded by the NIH for over 25 years, securing over $18 million in grants as a Principal Investigator. Additionally, Professor Zong is actively involved in editorial roles for several scientific journals, highlighting his significant contributions to cancer research and his leadership in the field.

Nitrogen Metabolism in Liver Cancer

ABSTRACT

The liver is the main organ that detoxifies ammonia – the primary nitrogenous waste produced from dietary proteins. Two major ammonia-detoxifying pathways in the liver are: 1) the urea cycle (UC) that converts ammonia into nontoxic urea for excretion; and 2) biosynthesis of glutamate and glutamine from ammonia. Genetic or pathological disruption of these ammonia-detoxifying mechanisms leads to hyperammonemia and neurotoxic symptoms. Recently, their critical roles in liver cancer have started to emerge. In hepatocellular carcinoma (HCC), the expression of the urea cycle enzymes (UCEs) is often down-regulated, whereas the expression of glutamine synthetase (GS) is upregulated. Using genetically engineered mouse models of hepatocellular carcinoma (HCC), the most common type of liver cancer, we study how the ammonia detoxifying mechanisms may play a role in cancer development and how they can be targeted for the mitigation of HCC.

Professor Hanming Shen

Chair Professor, Associate Dean (Teaching),
Faculty of Health Sciences,
University of Macau

BIOGRAPHY

Professor Han-Ming Shen is a distinguished researcher in the fields of health sciences and physiology, currently serving as Chair Professor and Associate Dean (Teaching) at the Faculty of Health Sciences, University of Macau. He has an extensive publication record in top-tier journals, including Autophagy, Cancer Research, and the Journal of Biological Chemistry. His research focuses on autophagy and lysosomal biology in cancer cell biology, mitophagy, and cancer metabolism, with significant contributions to understanding the molecular mechanisms of these processes. Professor Shen is recognized for his pioneering work in identifying novel pathways and regulators involved in autophagy, which have implications for targeted cancer therapies. He has received numerous awards for his academic achievements, including the NUS Medicine Researcher of the Year Award and the Faculty Research Excellence Award. Additionally, he plays a vital role in editorial boards for various scientific journals, contributing to the advancement of research in his field.

Novel Regulatory Mechanisms of Mitophagy: From Transcription to Post-translational Modifications of PINK1

ABSTRACT

Mitophagy is a selective form of autophagy for clearance of damaged mitochondria via the autophagy-lysosome pathway. Among various mitophagy regulatory mechanisms, PINK1, a protein kinase, and Parkin, an E3 ligase, are two critical players, with important implications in neurodegenerative disorders such as Parkinson's disease (PD). In this presentation, I will cover some of our recent work, including (1) Identification of a non-canonical function of SMAD3 as a novel nuclear transcription factor of PINK1; (2) effect of glucose-6-phosphate dehydrogenase (G6PD), a key enzyme in glycolysis, on PINK1; (3) Establishing *O*-*N*-acetylgalactosamine (*O*-GalNAc) of PINK1 as a novel form of post-translational modifications in control of PINK1 activation in response to acute mitochondrial damage. Our results thus provide a deeper insight into the molecular mechanisms in control of PINK1, the guardian of mitochondria and lay foundation for development of novel interventional strategies in PINK1 and mitophagy-related human diseases such as neurodegeneration and cancer.

Professor Yanxiang Zhao

Professor, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University

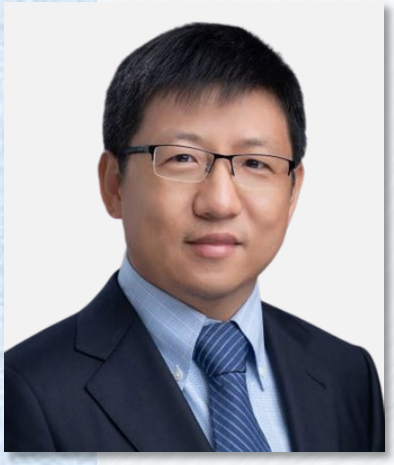
BIOGRAPHY

Professor Yanxiang Zhao is a distinguished researcher in applied biology and chemical technology, currently serving as a Professor at the Hong Kong Polytechnic University. She earned her Ph.D. from The Rockefeller University and has an extensive background in cellular signaling and autophagy. Prof. Zhao's research focuses on the functional mechanisms of cellular signaling proteins and the development of novel therapeutic strategies, particularly through autophagy-targeting peptides and immunotherapy for cancer treatment. She has published extensively in high-impact journals, including Nature Communications, Science Advances, and PNAS, contributing significantly to the understanding of autophagy's role in cellular homeostasis and disease processes. Her innovative work has led to the identification of critical interactions within autophagy pathways, providing insights into potential therapeutic applications. Prof. Zhao is also recognized for her leadership in academic service, serving as an ad hoc reviewer for multiple prestigious journals and participating in various research panels. Her contributions position her as a leader in the field of biomedical research.

The Beclin 1-Vps34 Molecular Machinery in the Autophagy Process: Structural Studies and Design of Novel Modulators

ABSTRACT

The Beclin 1-Vps34 complex is an indispensable molecular machinery in the autophagy process. Within this multi-subunit protein assembly, Beclin 1 recruits regulators such as Atg14L and UVRAG to form the coiled coil scaffolding arm while the lipid kinase Vps34 and its endogenous binding partner Vps15 forms the catalytic arm. The assembly of these two arms into a V-shaped structure that docks onto nascent pre-autophagosomal structure is essential for autophagy as the resulting active complex can generate PI3P lipids to promote autophagosome biogenesis. Our lab has determined the crystal structures of the coiled coil domain of Beclin 1, as well as its complex with the regulators Atg14L and UVRAG. Our structures reveal that the Beclin 1 coiled coil domain is structurally metastable due to many non-canonical pairings that destabilize the otherwise hydrophobic dimer interface. Atg14L and UVRAG readily dissociate the metastable homodimer of Beclin 1 and form stabilized Beclin 1-UVRAG and -Atg14L heterodimer through electrostatically complementary interactions at the coiled coil interface. Additionally, we also determined the structure for the coiled coil domain of NRBF2, a secondary modulator of the Atg14L-containing Beclin 1-Vps34 complex. Our structure shows that the oligomeric state of NRBF2 as mediated by its coiled coil domain is critical for strengthening its association with Vps15 and for promoting autophagy. Guided by our structural findings, we have developed a series of stapled peptides that selectively target the coiled coil domain of Beclin 1 to promote autophagy. These designed peptides showed potent autophagy-inducing effect in cell-based assays and inhibited tumor growth in animal-based cancer models. These results suggest the potential strategy to target autophagy-implicated human diseases such as cancer and neurodegeneration.



Professor Jiahong Lu

Associate Professor, Deputy Director (Research and Technology Transfer), Institute of Chinese Medical Sciences, University of Macau

BIOGRAPHY

Professor Jiahong Lu is an Associate Professor and Deputy Director at the Institute of Chinese Medical Sciences, University of Macau. He obtained his PhD from Hong Kong Baptist University in Hong Kong and completed his postdoctoral training at the Icahn School of Medicine at Mount Sinai in New York City, US. Since 2014, Dr. Lu has been working at the Institute of Chinese Medical Sciences, University of Macau, initially as an Assistant Professor and later as an Associate Professor. Dr. Lu's primary research interests revolve around autophagy biology and the pharmacological study of Chinese medicine. He has published more than 130 papers in prestigious journals such as Nature Biomedical Engineering, EMBO Molecular Medicine, Autophagy, APSB and others, accumulating over 13,000 citations. Dr. Lu has received several notable awards for his work, including the "Annual Young Scientist Award" from the TCM Brain Science Conference in 2022, and the Third Prize of Macau Natural Science Award in 2024. Furthermore, Dr. Lu actively contributes to the scientific community as an Editorial Board member for scientific journals including Acta Pharmaceutica Sinica B and Neurochemistry International.

Artificial Intelligence-assisted Discovery of Neuroprotective Autophagy Enhancers

ABSTRACT

Dysregulated autophagy is a central mechanism in brain aging, positioning brain-penetrating autophagy enhancers as promising therapeutic candidates for neurodegenerative disorders, such as Alzheimer's disease (AD). However, current enhancers primarily target the mTOR pathway, raising concerns on potential off-target and side effects due to mTOR's extensive physiological roles. In response to these challenges, here we developed DeepNAE (Neuroprotective Autophagy Enhancer), an AI-driven platform integrated with cross-species experimental validation, designed to rapidly identify mTOR-independent, blood-brain barrier (BBB)-permeable autophagy enhancers for AD therapy. Employing GPU-accelerated computational screening of 1.16 million compounds, DeepNAE conducted ultra-rapid, multi-tiered analyses, ultimately resulting in two lead compounds—Ombuin and 2-Hydroxycinnamic acid—for detailed evaluation in nematode and rodent AD models. Both compounds significantly reduced pathological protein aggregates (amyloid-β and phosphorylated tau), restored spatial memory, and improved learning capabilities. Liquid chromatography-tandem mass spectrometry confirmed their BBB penetration, aligning with our DeepNAE computational predictions. To promote broader research and development, we have made the DeepNAE platform open-source, enabling researchers to identify BBB-penetrant neuroprotective agents using their custom reference compound libraries. This study introduces a novel paradigm for AI-guided drug discovery, seamlessly integrating computational efficiency with robust cross-species validation to offer a scalable and effective approach for addressing autophagy dysregulation in neurodegenerative diseases.

Professor Juxian Song

Professor, School of Pharmacy, Chengdu University of Traditional Chinese Medicine

BIOGRAPHY

Professor Juxian Song is a prominent researcher in pharmacology and neurobiology, currently serving as a Professor at the School of Pharmacy, Chengdu University of Traditional Chinese Medicine. He holds a Ph.D. from the University of Hong Kong and has a strong academic background in both Chinese and Western medicine. His research focuses on the mechanisms of autophagy deregulation in neurodegenerative disorders and the pharmacological effects of traditional Chinese medicine in treating these conditions. Professor Song employs advanced techniques to investigate the therapeutic potential of acupuncture and natural compounds for neuroprotection. He has published numerous articles in high-impact journals, contributing significantly to the understanding of Alzheimer's and Parkinson's diseases. His work has garnered attention for identifying novel pathways and targets for drug discovery. Additionally, Professor Song is actively involved in teaching Chinese medicine pharmacology and neuropharmacology, highlighting his commitment to education and research in the field of neurodegeneration. His contributions have positioned him as a leading figure in the intersection of traditional and modern therapeutic approaches.

Acupuncture Alleviates Alzheimer's Pathology by Modulating Autophagy and Cellular Senescence

ABSTRACT

Alzheimer's disease (AD), the most prevalent neurodegenerative disorder (ND) leading to dementia, currently lacks a curative treatment. Autophagy impairments, neuroinflammation and cellular senescence are critical contributors to AD pathogenesis. Although acupuncture and electroacupuncture (EA) are widely employed as complementary therapies for treating neurodegenerative disorders like AD, their underlying mechanisms remain largely uncharacterized. We and collaborators demonstrated the multifaceted neuroprotective effects of EA therapies in AD transgenic mice. EA treatment efficiently rescued cognitive impairment and attenuated both Aβ and Tau pathology in animal models. Mechanistically, EA promotes the clearance of Aβ, Tau and NLRP3 inflammasome by activating TFEB/TFE3-mediated autophagy. In addition, EA also inhibits neuroinflammation via regulating cellular senescence. Collectively, our findings elucidate the molecular mechanisms underlying the therapeutic utility of EA as a non-pharmacological alternative for AD and other NDs.