Australian Government
Department of Industry, Innovation and Science

Australian Academy of Science

Chinese Academy of Sciences

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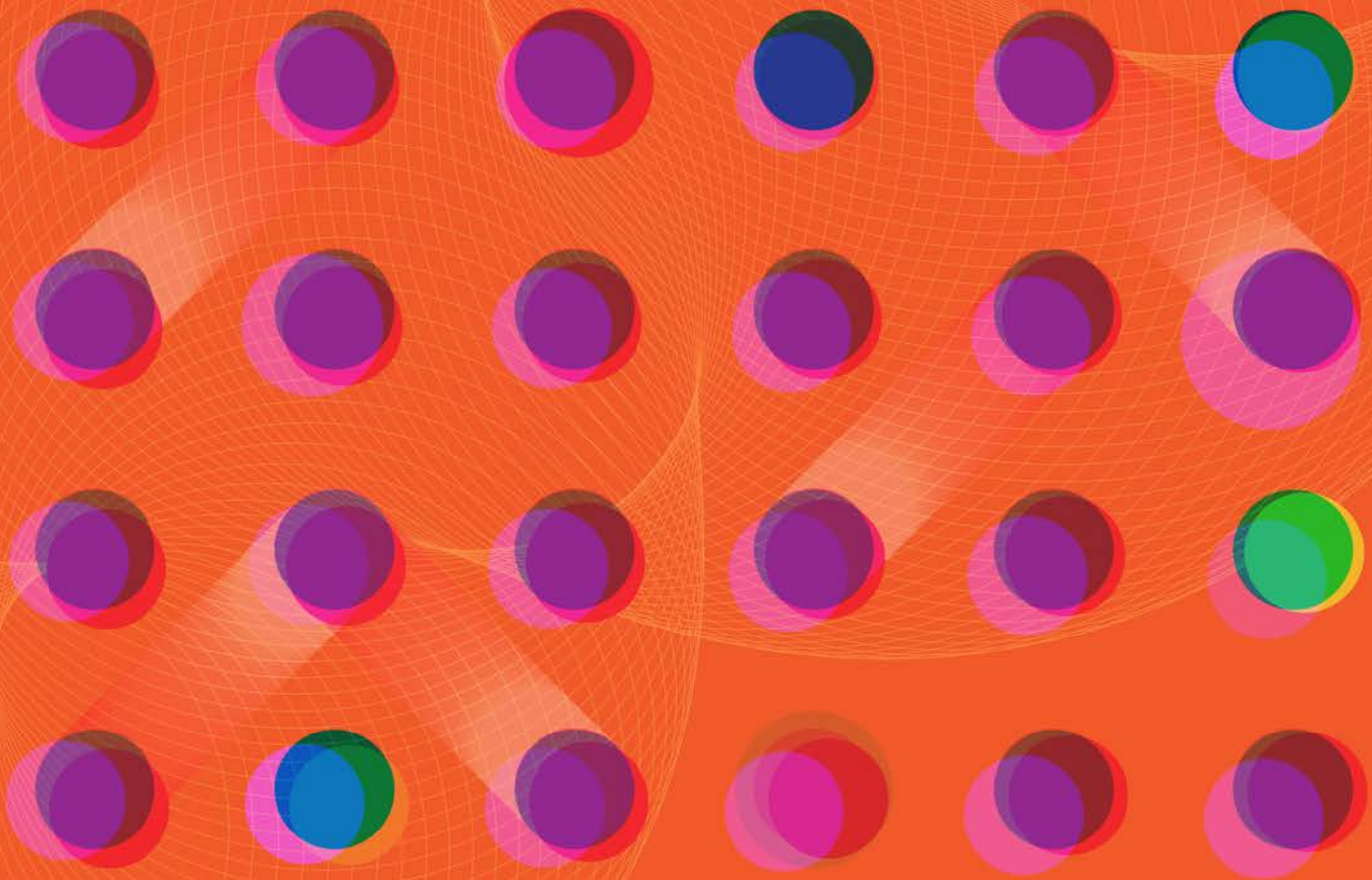
Australian Academy of Technology & Engineering

15th Australia–China Symposium

PRECISION MEDICINE



PROGRAM 6–8 NOVEMBER 2019 WERRIBEE, VICTORIA

Contents

Welcome

Since 2004 the Australian Academy of Science, the Australian Academy of Technology and Engineering (ATSE) and the Chinese Academy of Sciences (CAS) have held annual symposia on topics of strategic importance to both countries. These meetings provide an opportunity to build strong bilateral networks and increase research collaborations between Australia and China.

The Australian academies are pleased to host this year's symposium on the topic of precision medicine in Werribee, Victoria, from 6 to 7 November, with subsequent site visits in Melbourne on 8 November 2019. We welcome the Chinese and Australian researchers, including a cohort of early- and mid-career researchers from both countries, and thank them for attending this exciting meeting.

The Academies would like to thank Dr Anna Lavelle FTSE, Professor John Skerritt FTSE, and Professor Bob Williamson AO FAA FRS for agreeing to be on the Steering Committee of this event.

This symposium has been made possible with funding and support from the Australian Government Department of Industry, Innovation and Science, through the Australia–China Science and Research Fund, as well as the Chinese Academy of Sciences. We thank them for their continued support of this activity, which will enhance collaborations between Australia and China in the field of precision medicine.

Professor John Shine AC PresAA
President
Australian Academy of Science

Professor Hugh Bradlow FTSE
President
Australian Academy of Technology and Engineering

Program

Tuesday, 5 November 2019

Various times	**Australian and Chinese delegates arrive** Accommodation at Lancemore Mansion Hotel Werribee Park
1800–2030	**Arrival drinks and informal dinner** Pre-dinner canapes and drinks in the Snooker Room Dinner at the Heritage Veranda

Wednesday, 6 November 2019

0830	**Welcome and opening** Professor John Shine President Australian Academy of Science Professor Hugh Bradlow President Australian Academy of Technology and Engineering Mr Zhenyu Wang Deputy Director-General Chinese Academy of Sciences
0905	**Keynote presentation** *Precision medicine in China* Professor Wu Jiarui Shanghai Institutes for Biological Sciences
Session 1: Clinical practice of precision medicine	
0930	*Clinical practice of precision medicine* Professor Catriona McLean Alfred Health
0950	*Precision medicine in diabetes: prevention and treatment* Professor Weiping Jia Shanghai Jiao Tong University Affiliated Sixth People's Hospital
1010	*Integrating genomics into clinical practice: a local and global perspective* Professor Kathryn North Murdoch Children's Research Institute
1030	Morning tea
Session 2: Personalised drugs for cancers	
1050	*The coming of age of cell and gene therapies* Professor John Rasko University of Sydney
1110	*Exploiting metabolic vulnerability in cancer therapy* Professor Min Huang Shanghai Institute of Materia Medica
1130	*Discovery of a clinical candidate CYH33: a highly potent and selective PI3K alpha inhibitor for the treatment of advanced solid tumours in an era of precision medicine* Professor Linghua Meng Shanghai Institute of Materia Medica
1150	**Panel discussion: session 1 and 2**
1230	Working lunch
Session 3: Personalised drugs for central nervous system diseases	
1330	*The physiological and pathological roles of β-secretase (BACE1) during brain aging and neurodegenerative disorders* Professor Yong Shen Neurodegenerative Disorder Research Center
1350	*Towards the understanding of the genetic architecture of human complex traits* Professor Jian Yang University of Queensland
1410	*GV-971 inhibits Alzheimer's disease progression via remodelling gut microbiota* Professor Meiyu Geng Shanghai Institute of Materia Medica
1430	Afternoon tea
Session 4: Personalised drugs for metabolic diseases/disorders	
1450	*Development of personalised drugs for metabolic syndrome* Professor Jia Li Shanghai Institute of Materia Medica
1510	*Industry perspective on precision medicine* Dr Anna Lavelle
1530	*Novel intestinal targets for the treatment of obesity and NAFLD* Professor Cen Xie Shanghai Institute of Materia Medica
1550	**Panel discussion: session 3 and 4**
1630–1700	**Day 1 wrap up**
1800–1900	**Cocktail reception** Early- and mid-career researcher poster presentations The Pavilion
1900–2100	**Official symposium dinner** The Pavilion

Thursday, 7 November 2019

Session 5: Biomarkers and precision medicine	
0900	**Welcome** Professor Bob Williamson University of Melbourne
0910	*Proteogenomic analysis of HBV-related hepatocellular carcinoma* Professor Hu Zhou Shanghai Institute of Materia Medica
0930	*Genetic biomarkers for retinal disorders* Professor Melanie Bahlo Walter and Eliza Hall Institute of Medical Research
0950	*Integrative proteomics identifies cancer heterogeneity and new therapeutic opportunity* Professor Minjia Tan Shanghai Institute of Materia Medica
1010	Morning tea
Session 6: Technology innovations promote precision medicine	
1030	*Wearable sensing and medical big data* Professor Ye Li Shenzhen Institutes of Advanced Technology
1050	*The real deal: what works and what causes problems when implementing a major collaboration in big data research between China and Australia in eye health* Professor Mingguang He University of Melbourne
1110	*Innovation in action at AbbVie* Dr Laura Issa AbbVie Inc
1130	*Precision medicine: multi-omics-based novel biomarker discovery!* Professor Gaoxiang Ge Shanghai Institutes for Biological Sciences
1150	**Panel discussion: session 5 and 6**
1230	Working lunch

Session 7: Ethics, education and regulation	
1300	*Ethical, legal and social implications of new biomedical technologies: a case study on genome editing* Professor Dianne Nicol University of Tasmania
1320	*New systems advancing innovation in the Amendment of Drug Administration Law* Professor Yue Yang Shenyang Pharmaceutical University
1340	*Precision medicine: regulatory developments in Australia and globally* Professor John Skerritt Australian Government Department of Health
1400	Afternoon tea
1420	**Panel discussion: session 7**
1500–1530	**Symposium wrap up and farewell**
1830–2030	**Farewell dinner** The Pavilion Terrace

Friday, 8 November 2019

Before 0900	**Hotel check out** Breakfast available for overnight guests
0915	**Bus departs from Lancemore Mansion Hotel Werribee Park**
0915–1400	**Site visits for CAS delegation**
1600	**Bus 1 departs from the University of Melbourne Parkville Campus to Melbourne airport**
1930	**Bus 2 departs from the University of Melbourne Parkville Campus to Melbourne airport**

Speakers

Keynote speaker (China)

Professor Wu Jiarui

Shanghai Institutes for Biological Sciences

clchen@sibs.ac.cn

Professor Wu Jiarui graduated from the Department of Biology at Zhongshan University in Guangzhou in 1982. In 1985 he received a master's degree from the Institute of Genetics (CAS), and a doctorate in 1994 from the Federal Institute of Technology in Zurich, Switzerland. Later that year Professor Jiarui pursued his postdoctoral studies at the Health Science Center of the State University of New York.

Professor Jiarui has been engaged in cell molecular biology research at the Shanghai Institute of Biochemistry and Cell Biology (CAS) since 1997. He served as vice president of the Shanghai Institute of Life Sciences (CAS) from 2002 to 2012 and in 2005 became the first director of the Department of System Biology of University of Science and Technology of China. Professor Jiarui is the current dean of the School of Life Science and Technology at Shanghai University of Science and Technology, vice president of the Shanghai Institute of Advanced Studies (CAS), director of the Key Laboratory of System Biology (CAS) and vice chair of the Chinese Society of Biochemistry and Molecular Biology. He is an editor of the Journal of Molecular Cell Biology, associate editor of Frontiers in Systems Physiology, associate editor of BMC Systems Biology and deputy editor of the Science Committee of the United States.

Precision medicine in China

In the face of the grand challenges of complex diseases such as cancer and diabetes, researchers have developed precision medicines to identify new biomarkers for prediction of disease progression and accurate diagnosis of individuals. Discovery of biomarkers by precision medicine relies on two new approaches to analyse big data. Firstly, an approach for integrating big data derived from genomics, proteomics, metabolomics and other omics, and for integrating big data from molecular level to physiological and pathological levels. Secondly, an approach for building an individual-centric biomedical database that consists of multilayered and highly interconnected biological parameters, and then to construct a knowledge network of biomedical research that could be used for new taxonomic classification of diseases.

Session 1: Clinical practice of precision medicine

Professor Catriona McLean AO

Alfred Health

c.mclean@alfred.org.au

Professor Catriona McLean AO holds a number of academic qualifications: BSc (1979, University of Melbourne), MBBS (1984, University of Melbourne), FRCPA (1993), MD (1999, University of Melbroune), FFSc (2011, RCPA) 2011 and FAHMS (2016). She has published or has in press more than 430 peer-reviewed papers and 10 book chapters, which have been cited 22 129 times to date. In 2019 Professor McLean was ranked among the top 500 Australian scientists.

Professor McLean has made seminal, original and sustained contributions to the field of pathology, specifically in the fields of neuropathology and cancer medicine. In 2016, she was on the Australian Council of Learned Academies precision medicine scoping project. Professor McLean also serves as a professorial fellow at the Florey Institute of Neuroscience and Mental Health, director at the Victorian Neuromuscular Laboratory Service, chief pathologist at the Victorian Melanoma Service, consultant pathologist at the Australian Phenomics Network, professor at the Monash University Central Clinical School and has her main job as head of the anatomical pathology department at Alfred Health, where she oversees the diagnosis of 24 000 biopsies per year.

Clinical practice of precision medicine

Somatic mutation testing for cancer is now central to clinical practice. Mutation tests aim to:

- provide additional information to allow for an integrated WHO pathologic diagnosis
- find targetable mutations
- determine additional prognostic factors
- monitor disease.

Using recent practice examples, this talk will cover the clinical practice of precision medicine via mutation testing of cancers within a public hospital setting.

Professor Weiping Jia

Shanghai Jiao Tong University Affiliated
Sixth People's Hospital
wpjia@sjtu.edu.cn

Professor Weiping Jia is a professor at the Shanghai Jiao Tong University, immediate past president of the Shanghai Sixth People's Hospital (2010–18) and director of the Shanghai Institute of Diabetes. Professor Jia also served as the immediate past president of the Chinese Diabetes Society from 2016 to 2018 and has served as the director of the National Office for Primary Diabetes Care, chief editor for the Chinese Journal of Internal Medicine, associate editor for the Diabetes Research and Clinical Practice, as well as editorial board member the of Lancet Diabetes & Endocrinology.

Her research interest includes the diagnosis, monitoring and genetic risk factors of diabetes and abdominal obesity. She has established new diagnostic standards for diabetes and abdominal obesity for Chinese people, as well as discovered genetic susceptibility for type 2 diabetes in Chinese people and established the normal standard of continuous glucose monitoring. She has published over 250 research articles in international journals, including BMJ, Lancet Diabetes & Endocrinology, the Journal of the American College of Cardiology, Diabetes, Diabetes Care, Diabetologia, the Journal of Clinical Endocrinology and Metabolism and AJP, among others.

Precision medicine in diabetes: prevention and treatment

Type 2 diabetes mellitus (T2D) is a metabolic disease characterised by hyperglycaemia with complex aetiology. There are about 100 million adults with diabetes in China. Long-term hyperglycaemia may cause multiple organ injuries including stroke, blindness, myocardial infarction, renal failure and amputation. So far, the research and development of early warning and individualised treatment of diabetes is still a worldwide problem. Genetic markers can provide early warning information before obesity, abnormal glucose regulation and other clinical phenotypes appear. Therefore, we aim to analyse the genetic aetiology of T2D and investigate early genetic markers for its occurrence and development in the Chinese population for the guidance of clinical prevention and individualised treatment.

We carried out large-scale genetic researches of T2D in Chinese Han population. We validated 28 European-derived T2D susceptible loci and identified 12 novel susceptible genes in Chinese people. Moreover, we constructed the genetic risk score model for T2D based on the 40 genetic loci previously identified in Chinese population and reported the predictive value of the genetic model in prospective cohorts. The construction of the model is of great value to reveal the aetiology and early warning of T2D in Chinese. In addition, we performed pharmacogenomics studies and discovered that the T2D susceptibility genes can also be used to estimate the hypoglycaemic drug response. We found that PAX4 and KCNQ1 can be used to determine the efficacy of repaglinide and rosiglitazone, respectively. Based on the single genetic markers on drug efficacy, we also constructed two genetic scoring models for repaglinide and rosiglitazone drug efficacy, respectively. The model can be used to estimate the responses of different drugs.

Professor Kathryn North AC

Murdoch Children's Research Institute
kathryn.north@mcri.edu.au

Professor Kathryn North AC is trained as a paediatric physician, neurologist and clinical geneticist and was awarded a doctorate for her research in neurogenetics. She also completed a postdoctoral fellowship in the Harvard University genetics program.

Professor North is a national and global leader in genomic medicine. She leads Australian Genomics, a national network of 80 institutions around Australia funded by the National Health and Medical Research Council that has the goal of developing evidence and practical strategies to embed genomic medicine in the health system. She is vice chair of the Global Alliance for Genomics and Health, a collaborative network of over 500 organisations across more than 90 countries.

Professor North served as a chair of the NHMRC Research Committee from 2012 to 2018. She has received a number of awards for her research, including the GSK Award for Research Excellence, and in 2019 she was awarded a Companion of the Order of Australia in recognition of her eminent service to genomic medicine and medical research.

Integrating genomics into clinical practice: a local and global perspective

Australian Genomics is a National Health and Medical Research Council-funded national collaborative network committed to implementing genomic medicine within Australia and providing evidence to inform policy and practice. Australian Genomics comprises over 80 partner organisations, including the diagnostic pathology and clinical genetics services of all Australian states and territories, along with the major research and academic

institutions and peak professional bodies. Australian Genomics has four major work programs oriented around different challenges to integrating genomic medicine into Australian health care. These comprise a national diagnostic and research network; a federated data infrastructure; a focus on regulatory, economic policy and examination of the barriers to implementation; and an education, ethics and workforce focus. Our clinical programs are currently piloting genomic medicine for patients with rare diseases or cancers across multiple Flagships. Each Flagship project is examining the clinical utility of a variety of genomic sequencing technologies and using the resulting data to support data sharing and inform the regulatory, ethical, economic, policy and workforce infrastructure required to integrate genomics as a key part of the Australian health system. The Australian Functional Genomics Network aims to build collaborative links between Australian clinicians discovering variants or candidate novel disease genes of unknown significance with researchers who can investigate functional consequences of the gene/variants.

Australian Genomics is also a leading member and driver project of the Global Alliance for Genomics and Health, an organisation of over 500 of the world's leading biomedical research institutions, healthcare providers, information technology and life science companies, funders of research, and disease and patient advocacy organisations. The Global Alliance aims to accelerate the world-wide effort to responsibly aggregate, analyse and share large amounts of genomic and clinical information to advance the understanding, diagnosis and treatment for cancer, inherited diseases, infectious diseases and drug responses.

Session 2: Personalised drugs for cancers

Professor John Rasko AO

University of Sydney

j.rasko@centenary.usyd.edu.au

Professor John Rasko AO is an Australian pioneer in the application of adult stem cells and genetic therapy. Since 1999 he has directed the Department of Cell and Molecular Therapies at Royal Prince Alfred Hospital and the Gene and Stem Cell Therapy Program at the Centenary Institute in the University of Sydney. He is the president (2018–20) of the prominent International Society for Cell and Gene Therapy. Professor Rasko is a clinical haematologist, pathologist and scientist with an international reputation in gene and stem cell therapy, experimental haematology and molecular biology. In over 170 publications he has contributed to the understanding of stem cells and blood cell development, gene therapy technologies, cancer causation and treatment, human genetic diseases and molecular biology. Professor Rasko is a founding fellow of the Australian Academy of Health and Medical Sciences. In 2018, the board of the ABC honoured him as the 60th Boyer Lecturer. He is the recipient of national (RCPA, RACP, ASBMB) and international awards in recognition of his commitment to excellence in medical research, including appointment as an Officer of the Order of Australia.

The coming of age of cell and gene therapies

A possible 900% increase in gene and stem cell therapy approvals has been forecast for the next five years. Immunotherapies, including checkpoint inhibitors and CAR-T cells, have captured the attention of many scientists, physicians and cancer sufferers. The convergence of substantial incremental technical advances towards combined cell and gene therapy has led to improved clinical outcomes in immune deficiencies, haemoglobinopathies, blindness, immunotherapies and other inherited diseases. Our audit of cell, tissue and gene products with marketing authorisation in 2018 identified 44 unique products worldwide; 37 of them are cell and tissue therapies (84%) and mainly autologous (55%). The challenge of realising the full potential of genetic understanding has been in overcoming the hurdles of efficient gene therapy. Since the first human clinical trial using gene technology in 1989, there have been nearly 3000 approved clinical trials worldwide. The overwhelming majority of human clinical trials involves short-term gene expression or random integration of a therapeutic gene. Emerging technologies require controlled development in compliance with safety, regulatory and GMP requirements. Highlights in the clinical cell and gene therapy field will be discussed with special reference to haemophilia, thalassemia, graft versus host disease and cancer.

In parallel with objectively proven therapies, 'stem cell tourism' has become a billion-dollar industry, with increasing examples of false claims. Embryonic and induced pluripotent stem cells have been mired in controversy and clinical development has been forestalled. We reported an analysis of the global distribution of more than 400 unique businesses marketing stem cell-based interventions. Many of these online entities promote clinical applications of 'stem cells' beyond present-day standards of care. These data should be of immediate concern to governments and ethicists being lobbied to amend laws governing the manufacture, distribution and clinical use of human cell-based medical products. Unregulated, untested or unsafe stem cell 'therapies' place the field at a difficult crossroad. Blurring the lines that distinguish evidence-based cell therapies from those that are not remains a fundamental public health concern.

Professor Min Huang

Shanghai Institute of Materia Medica
mhuang@simm.ac.cn

Professor Min Huang received her PhD from the Shanghai Institute of Materia Medica (CAS) in 2007 and undertook her postdoctoral training at the Dana-Farber Cancer Institute at the Harvard Medical School from 2008 to 2011. Professor Huang is currently working as faculty at the Shanghai Institute of Materia Medica.

Professor Huang's research interest is in exploiting metabolic vulnerability for cancer therapy. She is dedicated to discovering small molecule inhibitors to target metabolic enzymes and to identifying metabolic dependency of oncogene-driven cancers, thereby precisely directing metabolic inhibitors to oncogene-driven cancer.

Professor Huang has published over fifty peer-reviewed research articles in journals, including Cell, Cancer Cell, Molecular Cell and Nature Communications, and holds over 20 patents. She is recipient of a number of distinguished awards and honours.

Exploiting metabolic vulnerability in cancer therapy

Metabolic reprogramming, a hallmark of cancer, presents the new therapeutic opportunities and attracts increasing efforts in anti-cancer drug discovery. One of the biggest hurdles for the development of metabolism-targeted therapies is to identify the responsive tumour subsets, as the metabolic vulnerabilities for most human cancers remain unclear. This may largely explain the very limited benefits obtained in the clinical modalities of metabolic targets, in which metabolic inhibitors are often delivered broadly, to cancer patients without an indication of metabolic dependency. Facing this challenge, we took a strategy to establish the link between metabolic signatures and the well-defined oncogenic drivers. By integrating metabolomics and transcriptomics, we discovered that the activation of oncogenic drivers, such as receptor tyrosine kinases, causes distinct metabolic preferences. Genomic status of receptor tyrosine kinases may inform the precision therapy of metabolic inhibitors; our work provides the basis for patient stratification in metabolism-targeted therapies.

Professor Linghua Meng

Shanghai Institute of Materia Medica
lhmeng@simm.ac.cn

Professor Linghua Meng obtained her bachelor's degree in biology at the East China Normal University in 1996 and received her PhD in pharmacology from the Shanghai Institute of Materia Medica in 2001. She continued her training in oncology at the National Cancer Institute in the US for five years until she joined the Shanghai Institute of Materia Medica in 2006 as a professor in tumour pharmacology. Her research focuses on discovery and research on innovative anti-cancer drugs targeting phosphatidylinositol 3-kinaseα isoform (PI3Kα)/mTOR pathway and tumour immunology, as well as therapeutic strategies based on newly developed anti-cancer drug candidates. Professor Meng has published more than 70 research articles in SCI-cited journals and holds 25 domestic and international patents. She has been granted about 10 domestic and international academic awards to date, including the National Natural Science Award (second degree, 2009), Shanghai Science and Technology Award (first degree, 2008), the Servier Young Investigator in Pharmacology (2008) and the AACR Annual Meeting Scholar-in-Training Award (2004 and 2005).

Discovery of a clinical candidate CYH33: a highly potent and selective PI3K alpha inhibitor for the treatment of advanced solid tumours in an era of precision medicine

Phosphatidylinositol 3-kinaseα isoform (PI3Kα) is frequently deregulated in a wide variety of human solid tumours. Targeting PI3Kα has exhibited mild and variable responses in preclinical and clinical settings. In an effort to discover new PI3α inhibitors, CYH33 was identified as a novel PI3Kα-selective inhibitor with a distinctive structure, which is currently in clinical trials. CYH33 potently restrained tumour growth in mice that bear the human breast cancer cell xenografts and in R26-Pik3caH1047R; MMTV-Cre transgenic mice. CYH33 significantly inhibited proliferation of a panel of human breast cancer cells, while diversity in sensitivity was observed. Harbouring cells were activating PIK3CA mutation; the amplified HER2 were more responsive to CYH33 than their counterparts. Additionally, HER2-enriched or luminal subtype cells were more sensitive to CYH33 than basal-like breast cancer. Sensitivity to CYH33 was further revealed to be associated with induction of G1 phase arrest and simultaneous inhibition of Akt and ERK. Sensitivity of patient-derived xenograft to CYH33 was also positively correlated with a decrease in phosphorylated ERK. Taken together, CYH33 is a

promising PI3Kα inhibitor for breast cancer treatment. A decrease in ERK phosphorylation may indicate its efficacy, which will provide useful clues for rational design of the ongoing clinical trials.

Session 3: Personalised drugs for central nervous system diseases

Professor Yong Shen

Neurodegenerative Disorder Research Center

yongshen@ustc.edu.cn

Professor Yong Shen received his Bachelor of Science in physiology from Nanjing University in 1983. He received his master's in science in neurophysiology from the Shanghai Institute of Physiology (CAS) in 1986 and received his PhD in psychobiology and neuroscience from the State University of New York at Binghamton in 1989. He was a postdoctoral fellow at the National Institute of Mental Health at St. Elizabeths Hospital with the Johns Hopkins University School of Medicine from 1989 to 1990. He worked as a senior molecular neuropharmacologist in Abbott Laboratories from 1993. From 1998 to 2010, Professor Shen was an adjunct professor at Arizona State University. In 1997 he was promoted to chief professor of neurology and senior scientist at the L.J. Roberts Center for Alzheimer's Research and in 2009 he received the Changjiang Scholar Award by the China Ministry of Education.

Professor Shen also served as a senior scientist and director at the Center for Advanced Therapeutic Strategies for Brain Disorders from 2010 to 2014, and in 2014 he established the Brain Bank and Neurodegenerative Disease Research Center, which he devoted to combining basic research on mechanisms of cognition and neuron functions in the healthy brain with various brain disorders. That same year, Professor Shen received the Thousand Talents scholar award. He was also the recipient of the Zenith Award from Alzheimer's Association in 2007 and the Dutch Outstanding Research Scientist Scholarship by Royal Academy of Sciences in 1988.

The physiological and pathological roles of β-secretase (BACE1) during brain aging and neurodegenerative disorders

β-site amyloid precursor protein cleaving enzyme (BACE1) is an aspartic proteinase that has multiple functions in various physiological processes, such as cell differentiation, immunoregulation, and cell death. In 1999 BACE1 was simultaneously discovered by five groups using different experimental approaches to identify exactly the same protein. An increasing amount of evidence shows that BACE1 activity is present in many diseases, including Alzheimer's disease, schizophrenia and epileptic behaviour. However, a deeper understanding of the molecular biology of BACE1 is unclear in term of physiological functions. I will share some of the exciting progress in this aspect from my laboratory, such as the enzymatic properties, structure, biosynthesis and physiological functions, to provide a new perspective and rational assessment of drug ability. I will then discuss proposed strategies to control BACE1 activity for possible therapeutic application.

Professor Jian Yang

University of Queensland

jian.yang@uq.edu.au

Professor Jian Yang is a professor of statistical genomics at the Institute for Molecular Bioscience at the University of Queensland. He received his PhD in 2008 from Zhejiang University in China before undertaking postdoctoral research at the QIMR Berghofer Medical Research Institute in Brisbane. He joined the University of Queensland in 2012. His primary research interests are developing novel statistical methods to better understand the genetic architecture of complex traits and diseases, to identify putative target genes and to improve the accuracy of genomic risk prediction using high-throughput genetic and genomic data.

He was the 2012 recipient of the Centenary Institute Lawrence Creative Prize in recognition of his contribution to solving the 'missing heritability' paradox. He was awarded the Ruth Stephens Gani Medal by the Australian Academy of Science for distinguished research in human genetics in 2015 and the 2017 Prime Minister's Prize for Science Frank Fenner Prize for Life Scientist of the Year. He was named in the 2018 Clarivate Highly Cited Researchers and has published a career over 140 papers (including 32 ESI Highly Cited Papers) to date that have received more than 36 000 citations (Google Scholar, August 2019).

Towards the understanding of the genetic architecture of human complex traits

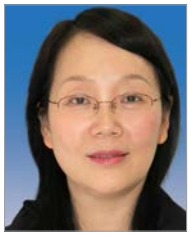
Most traits in humans, including neuropsychiatric disorders, are complex because they are influenced by many genetic, as well as environmental, factors. Understanding the genetic architecture of complex traits is of crucial importance for human health and evolutionary biology. In this talk, I will show the use of single nucleotide polymorphism data from genome-wide association studies (GWAS) to model the genetic architecture of complex traits and disorders. I will discuss

methods and analyses to detect signatures of natural selection that have shaped the genetic architecture. I will also demonstrate an analytical approach that integrates data from GWAS and large-scale genetic studies of molecular phenotypes (such as gene expression and DNA methylation) to predict putative causal genes and the likely mechanisms underpinning complex trait variation.

Professor Meiyu Geng

Shanghai Institute of Materia Medica

mygeng@simm.ac.cn



Professor Meiyu Geng's research is dedicated to innovative drug discovery and development for Alzheimer's disease (AD) and cancer, and exploring the diseases' mechanisms to guide the development of effective therapies. She has championed the development of more than 10 innovative drugs, including the oligosaccharide anti-AD drug GV-971, which was marked as a clinical breakthrough. Professor Geng received a number of distinguished awards and honours for her contributions to drug discovery in China.

GV-971 inhibits Alzheimer's disease progression via remodelling gut microbiota

Despite the tremendous efforts made in the treatment of Alzheimer's disease (AD), the past decades have witnessed the continuous failure of β-amyloid (Aβ) or tau-centric therapeutic strategies in late-stage clinical trials, which impels the reconsideration of new therapeutic strategy for this complicated disease. Recently, increasing evidence has suggested the association between gut dysbiosis and AD progression, yet the role of gut microbiota in AD pathogenesis remains obscure. In our research we provided a potential mechanistic link between gut microbiota dysbiosis and neuroinflammation in AD progression. Using AD mouse models, we discovered that during AD progression, the alteration of gut microbiota composition leads to the peripheral accumulation of phenylalanine and isoleucine, which stimulates the differentiation and proliferation of pro-inflammatory T helper 1 (Th1) cells. The brain-infiltrated peripheral Th1 immune cells are associated with the M1 microglia activation, contributing to AD-associated neuroinflammation. Importantly, the elevation of phenylalanine and isoleucine concentrations and the increase of Th1 cell frequency in the blood were also observed in two small independent cohorts of patients with mild cognitive impairment due to AD. Furthermore, GV-971, a sodium oligomannate that has demonstrated solid and consistent cognition improvement in a phase 3 clinical trial in China, was found to be suppressing gut dysbiosis and the associated phenylalanine/isoleucine accumulation, harnessing neuroinflammation and reversing cognition impairment. Together, our findings highlight the role of gut dysbiosis-promoted neuroinflammation in AD progression and suggests a novel strategy for AD therapy by remodelling the gut microbiota.

Session 4: Personalised drugs for metabolic diseases/disorders

Professor Jia Li

Shanghai Institute of Materia Medica

jli@simm.ac.cn

Professor Jia Li graduated from the Zhejiang Medical University's Department of Pharmacy in 1992. He entered the Shanghai Institute of Materia Medica (CAS) in 1994 and obtained a doctorate degree in science in 2000. Professor Li focuses his research mainly on three streams:

- discovery, evaluation and mechanism study of novel drug candidates that target metabolic diseases
- enzyme-based drug discovery
- mechanism study of cell fate regulation in a chemical-biology approach.

Professor Li has published 180 papers as the corresponding or co-corresponding author and is the co-inventor of 147 patents (with 70 already issued). His papers are published in various journals, such as Nature Communications, Advanced Materials, Diabetes, Diabetologia and the Journal of Biological Chemistry, with a H-index of 40 and more than 6700 total citations. Professor Li has led 15 pre-clinical studies, from which six drug candidates have successfully been transferred to domestic pharmaceutical companies. Two drug candidates have now entered phase 1 clinical trials.

Development of personalised drugs for metabolic syndrome

Type 2 diabetes (T2D), which is characterised by hyperglycaemia and insulin resistance, has become a global epidemic. In previous research, we were committed in the development of personalised hyperglycaemic drug candidates and therapeutic strategies to fulfil unmet clinical requests. Over the past five years we have been developing a potent and long-acting DPP-4 inhibitor (HL012) and drug candidate (DC81) to target SGLTs, which are now undergoing pre-clinical research.

In the personal therapeutic field, we identified a promising strategy by using the uncoupling of mitochondria and pyruvate dehydrogenase in

hyperglycaemia therapy. The uncoupling of mitochondria by the chemical uncoupler 2,4-dinitrophenol (DNP) is an efficient way to ameliorate hyperglycaemia and insulin resistance. However, DNP use ceased in the 1930s due to systemic toxicities including hyperlactacidemia, hyperthermia and even death. We identified an effect-enhancing and toxicity-reducing way of linking the activation of pyruvate dehydrogenase (PDH) with DNP to T2D therapy. Activation of PDH protected mice from DNP-derived fatality, hyperlactacidemia and hyperthermia and further promoted glucose disposal in diabetic mice. Based on the beneficial effects of PDH activation and uncoupling actions, a novel compound that showed both effects were identified and confirmed to promote glucose oxidation preferentially in vitro and in vivo.

Dr Anna Lavelle FTSE

alavelle@bigpond.net.au

Dr Anna Lavelle FTSE is an experienced non-executive director, who has served for over 25 years on the boards of not-for-profit, government and for-profit entities. She has a lengthy track record in healthcare delivery, technology development and negotiating government policy as both an executive director and non-executive director.

Dr Lavelle has a PhD in genetics from the University of Melbourne and is a graduate of the Australian Institute of Company Directors. She is a fellow of both the Academy of Technology and Engineering and of the Leadership Victoria program. Nature Scientific American Worldview ranked Dr Lavelle in the global top 100 'world visionaries' in biotechnology in 2015. She was the only Australian to be named.

From 2005 to 2016, Dr Lavelle was the CEO of AusBiotech Ltd, the national industry association for the biotechnology, pharmaceutical and medical devices sectors. Dr Lavelle is now serving on several boards, including as the independent chair of Medicines Australia, chair of Australia's National Digital Health Initiative, independent director of Soil CRC, chair of Avatar Brokers Ltd, non-executive director for Hemideina, Ministerial appointment on the National Health and Medical Research Council Innovation Committee and a member of the OUTBREAK Advisory Board.

Industry perspective on precision medicine

Professor Cen Xie

Shanghai Institute of Materia Medica
xiecen@simm.ac.cn

Professor Cen Xie graduated from the Shanghai Institute of Materia Medica (CAS) in 2013 with a doctoral degree and undertook postdoctoral training at the National Institutes of Health from 2013 to 2018. In October 2018, Professor Xie was appointed principal investigator and project leader of the Shanghai Institute of Materia Medica. Her current research interest is mainly on metabolic diseases and the discovery of novel therapeutic strategies for obesity, non-alcoholic fatty liver disease and diabetes. She applied integrative multi-omics approaches to tackle the question of cross-talking between the microenvironments of the intestine and liver, to investigate the mechanism of association between intestine and related diseases and to discover the new drug targets and innovative medical therapies. Professor Xie has published more than 50 papers, with many in the top of journals in the fields, including but not limited to Nature Medicine, Cell Metabolism and Nature Communications as first or co-first author, and those works have been cited more than 1000 times.

Novel intestinal targets for the treatment of obesity and NAFLD

Non-alcoholic fatty liver disease (NAFLD) is becoming the most common chronic liver disease in industrialised countries, with limited therapeutic options. NAFLD triggers an increased risk of non-alcoholic steatohepatitis (NASH) and end-stage liver diseases such as cirrhosis and, ultimately, hepatocellular carcinoma. Obesity is a well-recognised risk factor for NAFLD and efforts to control obesity would decrease NAFLD. However, direct therapies that target NAFLD or NASH remain extremely limited. A growing number of studies indicate that the gut microbiota, receptors in the intestinal epithelial cells and intestine-to-liver signalling axis modulate NAFLD.

Notably, our studies revealed that inhibition of the intestinal farnesoid X receptor (FXR) led to decreased obesity, insulin resistance and NAFLD in diet-induced and genetic models of metabolic disease. A second signalling pathway in the gut was examined by use of the intestine-specific knockout or activation. Chemical inhibition combined with lipidomic analysis revealed the intestinal HIF2α pathway that controls metabolic diseases, including NAFLD development. These studies found increased production of ceramides in the lower small intestine through the direct modulation of genes encoding ceramide synthesis enzymes. These studies have led to potentially new therapeutic strategies to control NAFLD by direct inhibition of receptors in the intestinal epithelial cells.

Session 5: Biomarkers and precision medicine

Professor Hu Zhou

Shanghai Institute of Materia Medica

zhouhu@simm.ac.cn

Professor Hu Zhou has interdisciplinary training in mass spectrometry and proteomics. He has been working in the areas of disease-related proteomics and systems biology for more than 10 years. His recent research has focused on studying proteomic research on drug target/mechanism discovery and translational medicine. Professor Zhou has served as a principal investigator and mass spectrometry facility director in the Shanghai Institute of Materia Medica (CAS). His group has published more than 50 peer-reviewed publications in the past five years.

Proteogenomic analysis of HBV-related hepatocellular carcinoma

We have performed the first proteogenomic characterisation of HBV-related hepatocellular carcinoma (HCC) using paired tumour and adjacent liver tissues from 159 patients. The integrated proteogenomic analyses revealed consistency and discordance among multi-omics, activation status of key signalling pathways and liver-specific metabolic reprogramming in HBV-related HCC. Proteomic profiling identified three subgroups associated with clinical and molecular attributes, including patient survival, tumour thrombus, genetic profile and the liver-specific proteome. These proteomic subgroups have distinct features in metabolic reprogramming, microenvironment dysregulation, cell proliferation and potential therapeutics. Two prognostic biomarkers, PYCR2 and ADH1A, related to proteomic subgrouping and involved in HCC metabolic reprogramming, were also identified. We revealed CTNNB1 and TP53 mutation-associated signalling and metabolic profiles, among which mutated CTNNB1-associated ALDOA phosphorylation were validated to promote glycolysis and cell proliferation. Our study provides a valuable resource that significantly expands the knowledge of HBV-related HCC and may eventually benefit clinical practice.

Professor Melanie Bahlo

Walter and Eliza Hall Institute of Medical Research

bahlo@wehi.edu.au

Professor Melanie Bahlo is a bioinformatician/statistical geneticist with over 20 years' experience working in the discovery of genetic basis of human diseases, with a focus on neurological disorders. Through leading the statistical genetics laboratory at the Walter and Eliza Hall Institute of Medical Research (WEHI) since 2007, her work combines the development of novel methods and successful applications in monogenic and complex diseases to identify and understand biological mechanisms perturbed in diseases. She co-established the WEHI Population Health and Immunity division and has recently been promoted to lead the Healthy Development and Ageing theme. Professor Bahlo has won two Australian science awards: the Moran Medal from the Australian Academy of Science in 2009 and the Genetics Society of AustralAsia's Ross Crozier Medal for mid-career researchers in 2015.

Genetic biomarkers for retinal disorders

Retinal disorders such as age-related macular degeneration and macular telangiectasia type II (MacTel) are late-age onset disorders and rising in prevalence due to our ageing populations. The disease risk for these disorders have both environmental and genetic contributions. The genetic risk factors have contributions from both rare variants—frequently associated with high risk but affecting few patients—and common variants associated with a probabilistic risk.

Determination of the genetic risk burden for patients could lead to a form of personalised medicine with the possibility of environmental risk modification for those patients. These genetic risk profiles biomarkers are not currently being applied to retinal disorder patients due to cost and lack of informativity for most patients. In MacTel, recent work has identified a genetic signature that is also identifiable with simple metabolic biomarkers. This, and the newly identified genetic risk profile, could also help diagnose MacTel, which remains a challenge, particularly early in the disease course.

Professor Minjia Tan

Shanghai Institute of Materia Medica
mjtan@simm.ac.cn

Professor Minjia Tan obtained his PhD from the Shanghai Institute of Materia Medica (CAS), after which he received postdoctoral training at the University of Chicago. He is currently a principal investigator at the Shanghai Institute of Materia Medica. His lab focuses on the development of new mass spectrometry-based proteomics technologies, which he uses to characterise the roles of protein post-translational modifications in cellular physiology and diseases, and to explore new therapeutic approaches and biomarkers.

Integrative proteomics identifies cancer heterogeneity and new therapeutic opportunity

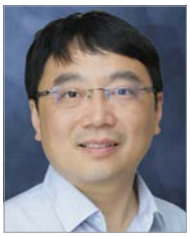
Comprehensive cancer genomics studies in the past decades have revolutionised our understanding of cancer biology and provided a new paradigm for cancer treatment through molecularly targeted therapies. Although genomic understanding of cancers is essential, functions and phenotypic characteristics are executed by proteins and regulated by protein post-translational modifications. Comprehensive characterisation of cancers at proteomics and PTMs level is therefore fundamental to better understand tumour biology, patient stratification and personalised therapy.

Using mass spectrometry-based proteomics approaches, we conducted large-scale molecular profiling of 103 clinical paired tumour and non-tumour lung adenocarcinoma tissues, including proteome profiling, phosphoproteome and whole-exome sequencing. The integrative analysis revealed three proteomic subtypes with distinct clinical outcomes, genomic feature, signalling pathways and potential therapeutic targets. Our proteomic and phosphoproteomic analyses of 43 KRAS mutant human cancer cell lines identified three robust subsets that recapitulated histological, pathological and prognostic features of human cancers. In-depth analysis of phosphoproteomic data allowed us to identify a set of new drug combinations with therapeutic potential for KRAS mutant cancer. Together, our study provides resources to understand cancer heterogeneity and identify new therapeutic possibilities towards precision medicine.

Session 6: Technology innovations promote precision medicine

Professor Ye Li

Shenzhen Institutes of Advanced Technology
ye.li@siat.ac.cn



Professor Ye Li received his bachelor and master's degrees from the University of Electronic Science and Technology of China in 1999 and 2002, respectively. In 2006 he received his PhD from Arizona State University in the US. He joined the Shenzhen Institutes of Advanced Technology (CAS) in 2008 and has been working in the areas of wearable sensing and computing, and health big data analysis for more than 10 years. As well as over 140 papers, Professor Li has so far published 45 SCI-indexed journal papers as the first or corresponding author. These publications have been cited over 1734 times (Google Scholar) in total, and the top paper has been cited 158 times to date. There are 69 authorised patents (13 PCT) and six ITU and CCSA standard proposals admitted in eHealth. At present, eight of the patents have been transformed as enterprises and the transformation funds have exceeded one million dollars.

Wearable sensing and medical big data

Cardiovascular disease (CVD) is the leading cause of mortality. Studies have shown that most acute CVD events happened outside the hospital, which means that wearable and continuous monitoring of physiological signal is deemed necessary. Unfortunately, the existing wearable devices have some obvious limitations, such as low accuracy, high physical load, lack of smart analysis, etc. We have hence focused our research on wearable sensing and computing, and medical big data analysis to solve the requirements of miniaturisation, higher energy efficiency, low physical load capability, higher accuracy and intelligence of wearable devices. As a result, a low-power ECG chip and SpO2/PPG chips were developed; two of the wearable products were granted CFDA in 2016.

Based on the fusion of data models and hemodynamic mechanism models, we improved precision of the cuff-less blood pressure for individuals. We proposed the spatial-temporal heterogeneous fusion analysis theory for physiological signals based on attention mechanism, which improved the precision and accuracy in recognising nine types of cardiac arrhythmias. We applied the developed wearable devices and system in monitoring life signals of submariners in the *Jiaolong* deep manned submersible since 2013. Based on regional big data platform, a medical big data management and

analysis system was developed to provide aided decision-making information for health supervision and management departments in Shenzhen city.

Professor Mingguang He

University of Melbourne
mingguang.he@unimelb.edu.au

Professor Mingguang He is currently a professor of ophthalmic epidemiology at the University of Melbourne and the Centre for Eye Research Australia, the director of the WHO Collaborating Centre for Prevention of Blindness (Australia). He is the former associate director and professor of ophthalmology in the Zhongshan Ophthalmic Center at Sun Yat-sen University in Guangzhou, China. His research interests include clinical and epidemiological research, randomised clinical trials, twin studies, imaging technology and big data research. He ran the first glaucoma survey and twin registry in China.

Professor He has published more than 290 scientific articles in international peer-reviewed journals, including the Journal of the American Medical Association and the Lancet, as well as important book chapters, with more than 11 900 citations. He has given more than 90 invited lectures at regional Asian and international conferences. He serves as editorial board member for several important journals, including Ophthalmology, the top ranked ophthalmology journal. Professor He has received several awards, including a distinguished young scholar award from the National Natural Science Foundation of China (2011) and the Holmes Lecture Award from the Asia-Pacific Academy of Ophthalmology (2015). He has received multiple major research grants both in China and Australia, including a Partnership Project Grant (2018) and Investigator Grant (2019) from the National Health and Medical Research Council.

The real deal: what works and what causes problems when implementing a major collaboration in big data research between China and Australia in eye health

I had been working in China for 20 years before joining the University of Melbourne faculty as a professor of ophthalmic epidemiology at the end of 2014. Since then, I have established the Australia China Health Accelerator, a big data consortium between Australia and China that has collected more than 200 000 clinical and imaging data for big data and artificial intelligence research and development. In this lecture, I will share my experiences in handling the opportunities and challenges in sharing data and further translating the discoveries into community benefits in Australia and China.

Dr Laura Issa

AbbVie Inc
laura.issa@abbvie.com

Dr Laura Issa is leading the Business Development, Search and Evaluation in Australia and New Zealand for AbbVie Inc, a global specialty biopharmaceutical company. Dr Issa is passionate about life science, healthcare innovation, access equality and quality use of medicines. She bridges science and business, having worked across the academic, biotechnology and pharmaceutical sectors, at all stages of the product life cycle to build value-based partnerships that advance medical research and innovation. Prior to joining AbbVie, Dr Issa held senior roles in business development and licensing at Aspen Pharmacare and Merck Sharp & Dohme, where she led projects across all therapeutics areas and executed partnership deals with local, regional and global companies. Prior to transitioning to the pharmaceutical industry, Dr Issa was a senior technology transfer and licensing professional with NewSouth Innovations. Dr Issa achieved a PhD from the Garvan Institute of Medical Research in 1999 and a Master of Business Administration (Technology) in 2005. She is a graduate of the Australian Institute of Company Directors and sits on the board of the Ruby Red Foundation.

Innovation in action at AbbVie

AbbVie is a global research and development-based biopharmaceutical company committed to developing innovative advanced therapies for some of the world's most complex and critical conditions. The company's mission is to use its expertise, dedicated people and unique approach to innovation to markedly improve treatments across four primary therapeutic areas: immunology, oncology, virology and neuroscience. In more than 75 countries, AbbVie employees are working every day to advance health solutions for people around the world. I will present ways in which AbbVie is leveraging technology and advanced analytics to improve precision and likelihood of success along the research continuum from discovery through to development.

Professor Gaoxiang Ge

Shanghai Institutes for Biological Sciences
gxge@sibcb.ac.cn

Professor Gaoxiang Ge obtained his PhD at the Shanghai Institute of Biochemistry and Cell Biology (CAS) and pursued his postdoctoral training at the University of Tennessee Health Science Center and the University of Wisconsin School of Medicine and

Public Health. Professor Ge returned to the Shanghai Institute of Biochemistry and Cell Biology (CAS) in 2007 to join as faculty. He is now the deputy director of the State Key Laboratory of Cell Biology and the vice chair of the Chinese Society of Matrix Biology. Professor Ge's laboratory focuses on the cell-extracellular matrix crosstalk in tissue homeostasis and diseases. Professor Ge's laboratory has recently extended its research to integrated multi-omics-based novel biomarker discovery for cancer therapy.

Precision medicine: multi-omics-based novel biomarker discovery!

Cancer is a highly heterogeneous disease. Despite the progress of targeted therapy and immune therapy, many patients are not responsive to anti-cancer therapies. In-depth understanding of the personalised characteristics of the highly heterogeneous cancer patient population is a prerequisite for achieving precision medicine. Patient-derived xenograft (PDX) models recapitulate the heterogeneity and diversity of the human patient population and offer the most translational preclinical model for anti-cancer drug screening. We have recently established a PDX and multi-omics-based biomarker discovery pipeline. The data integrated in the analysis included:

- responsiveness of PDX models to drugs
- genomic, transcriptomics and proteomics profiles
- functional status of the signalling pathways that are critical in cancer development, especially the expression, post-translational modification and spatial localisation of the key regulatory molecules and effect molecules.

AL3810 is an inhibitor to FGFR, VEGFR and PDGFR that is currently in clinical trial. AL3810 potently inhibits liver cancer PDX tumour growth. Compared to AL3810-resistant tumours, AL3810-sensitive tumours have high aerobic glycolysis activity. Liver cancers with high PKM2 expression are more sensitive to AL3810 in both PDX models and in vitro 3D co-culture with fibroblasts. Thus, PKM2 is a promising biomarker that may predict AL3810 efficacy.

Session 7: Ethics, education and regulation

Professor Dianne Nicol

University of Tasmania
dianne.nicol@utas.edu.au

Dianne Nicol is a professor of law and director of the Centre for Law and Genetics at the University of Tasmania. The broad theme of the centre's research is the interface between law, ethics, science and society in regulation and governance of genomics and related technologies. The centre was established 25 years ago and currently numbers over 17 faculty, research fellows, PhD candidates and assistants. Dianne leads two projects funded by the Australian Research Council; one on the legal matters, research ethics and social issues associated with genomic data sharing, and the other on the regulation of innovative health technologies.

Dianne has a PhD in cell biology and a Master of Laws on patenting of biotechnology inventions. She is a fellow of the Australian Academy of Law and was awarded the title Distinguished Professor in 2019. Dianne is also involved in a number of national initiatives on genomics and other health-related technologies.

Ethical, legal and social implications of new biomedical technologies: a case study on genome editing

From the beginning of the Human Genome Project in 1990 it was recognised that new developments in genetics (and what was to become genomics) raised significant ethical, legal and social implications (ELSI). For this reason, up to 5% of Human Genome Project funding was dedicated to ELSI research. As genomic technologies have developed, the ELSI have become even more profound. Genome editing technology in particular is requiring us to scrutinise our ethical norms and social values more closely, and examine the role of law and other forms of regulation in addressing these concerns. In this presentation, I will focus particularly on the ELSI of germline genome editing, highlighting the diversity of approaches to its regulation internationally and the desirability of a more coordinated approach.

Professor Yue Yang

Shenyang Pharmaceutical University
yyue315@vip.126.com

Professor Yue Yang is the director of the International Food and Drug Policy and Law Research Center at Shenyang Pharmaceutical University. She is a member of the 14th Academic Degree Evaluation Committee at the university and a chair of the Division of Pharmaceutical Administration. In 2004 she received her PhD and became the first doctorate in pharmacy administration in China, presiding over 78 scientific research projects on policy and regulations.

As a member of the Experts Group Revision of the Drug Administration Act, she participated in legislative research during the formulation of the Vaccine Administration Act. Professor Yang also participated in drafting and evaluating policy in the pilot scheme of the Marketing Holder System.

New systems advancing innovation in the Amendment of Drug Administration Law

I will briefly introduce the Amendment of Drug Administration Law and introduce several key articles on advancing innovation, including the marketing authorisation system, clinical trial review reform, accelerate review and others. I will discuss and propose some suggestions about opportunities and challenges that we may encounter when launching new drugs in China.

Professor John Skerritt FTSE

Australian Government Department of Health
john.skerritt@health.gov.au

Professor John Skerritt FTSE is a deputy secretary with the Australian Government Department of Health. He has line responsibility for the Therapeutic Goods Administration and the Office of Drug Control. The Therapeutic Goods Administration is Australia's regulator of medicines, medical devices (including IVDs), blood and cell and tissue therapies. Professor Skerritt has led the development of new regulatory frameworks for emerging technologies, including a regulatory framework for precision medicine products and development of a companion diagnostics scheme.

Professor Skerritt is an adjunct full professor in medicine, pharmacy and agriculture at the University of Sydney, University of Canberra and University of Queensland. He holds a first-class honours degree and a PhD in pharmacology. Professor Skerritt is the author of almost 300 publications, including 10 patents, many of which are related to diagnostic technologies. He was formerly a deputy secretary with the Victorian Government, deputy CEO of a Commonwealth Statutory Authority in the foreign affairs portfolio, a senior research manager in the Commonwealth Scientific and Industrial Research Organisation and involved in an industry joint venture partnership. This has included over 20 years of leading scientific and technical cooperation activities with China.

Precision medicine: regulatory developments in Australia and globally

Approval by the Therapeutic Goods Administration is required before any new medicine or diagnostic test can be marketed in Australia. As for all therapeutic goods, the same considerations of quality, safety and efficacy apply for precision medicine products, which can encompass development of targeted therapies, gene editing technologies and genomic tests, including those for biomarkers. Several additional issues arise for the regulation of precision medicine products. Often, use of the product is integrated with the delivery of a medical service. As well as an understanding of the clinical utility of a product, integration of precision medicine into health care requires new skills, systems and investments. There are ethical and logistic challenges arising from collection, storage, use and management of genomic data, to the impact of the result on the patient and because some gene therapies may irreversible.

Regulation touches on all of these issues. Apart from discussing the types of precision medicine products and how they are regulated, this presentation will cover the development of a new framework for regulation of companion diagnostics and for self-tests, including genetic tests. A new support service has been launched as precision medicine product developers are often small and medium-sized enterprises or researchers unfamiliar with regulatory requirements.

Symposium co-convenor

Professor Bob Williamson AO FAA FRS

University of Melbourne
r.williamson@unimelb.edu.au

Professor Bob Williamson AO FAA FRS made significant and fundamental contributions to human genetics. His early studies and polysomes helped to establish the existence of mRNA in mammalian cells. He led research into the molecular genetics of the thalassaemias and was the first to clone the human globin genes as cDNAs in 1977. This led to gene mapping for thalassaemias, muscular dystrophies and cystic fibrosis, as well as identifying the mutations causing Alzheimer's disease and myotonic dystrophy. He attempted gene therapy in 1994, using liposomes to introduce genes for CFTR in a clinical trial with cystic fibrosis patients in London. He is a fellow of the Royal Society, the Australian Academy of Science, the UK Academy of Medical Sciences, the Australian Academy of Health and Medical Sciences and of several medical royal colleges.

Poster presenters

Professor Daming Gao

Shanghai Institutes for Biological Sciences
dgao@sibcb.ac.cn

Professor Daming Gao received his PhD from the Institute of Biochemistry and Cell Biology of the Shanghai Institutes for Biological Sciences (CAS) in 2006. He was a postdoctoral fellow in the Department of Pathology in the Harvard Medical School from 2006 to 2010, and an instructor there from 2010 to 2012. Professor Gao returned to China and has been at the Institute of Biochemistry and Cell Biology (CAS) as a professor and group leader since 2012.

His overall scientific goal is to understand how mammalian cells sense and respond to environmental stimulations and how deregulation of such mechanisms contributes to cancer occurrence and progression. His current research interest primarily focuses in the field of cell signalling transduction, particularly understanding how deregulated signalling events could affect malignant transformation, cancer cell proliferation and metabolism. These changes are known characteristics that enable cancer cells to take advantage of the host system and develop into serious diseases.

Implication of deregulated CRL5 complex in cancer therapy

Ubiquitin-proteasome system is important for cellular protein homeostasis. Cullin5 (CUL5) associates with suppressor of cytokine signalling (SOCS) box proteins and other essential factors to form functional CRL5 E3 ligases. Although several substrates of CRL5 have been identified recently, little is known about how CRL5 E3 ligases function in cell signalling transduction. Recently, we identified the CUL5-SOCS3 E3 ligase complex that degrades integrin β1, which suppresses downstream FAK/SRC signalling and eventually inhibits lung cancer metastasis. Moreover, we further found that CUL5-SOCS6 E3 ligase complex targets Sin1, the core component of mTORC2 complex, for degradation. This process further decreases AKT phosphorylation and promotes cancer cell apoptosis. These results revealed important roles of CRL5 E3 ligases in modulating key signalling pathways of cancer cells and provides insights for developing new cancer therapy strategies by targeting Cullin5.

Professor Zhaobing Gao

Shanghai Institute of Materia Medica
zbgao@simm.ac.cn

Professor Zhaobing Gao received his PhD from the Shanghai Institute of Materia Medica (CAS) in 2006 and undertook postdoctoral training at the Johns Hopkins University in the US. He returned to China and was appointed to the faculty of the Shanghai Institute of Materia Medica in 2010. His research mainly focuses on ion channels involved in neuronal hyperexcitability disorders such as epilepsy and neuropathic pain, with major interest in identifying new functions and modulation mechanisms of ion channels. Professor Gao has two drug candidates for epilepsy that are currently in phase 1 clinical trials.

Discovery of a novel antiepileptic drug targeting KCNQ channels

Epilepsy is one of the most common, serious neurological disorders, affecting about 1% of the world's population and characterised by recurrent seizure attacks. Being a neuronal Kv7 channel activator, retigabine (RTG) has been approved for the treatment of epilepsy. However, the less than ideal distribution of RTG reduces its antiepileptic efficacy and increases potential non-CNS side effects. In addition, skin discolouration on peripheral tissues like nails and/or retinal pigment abnormalities was reported among some patients, presumably due to the chemical instability inherited by RTG's triaminobenzene structure. The supply of RTG has been discontinued in markets since June 2017. Pynegabine (HN37) was discovered after multiple rounds of structure modification of RTG. Pynegabine displays satisfied chemical stability and improved ratio of brain to blood. In addition, it exhibits an enhanced activating potency on Kv7 channels and a wider therapeutic window than RTG. Pynegabine is currently in phase 1 clinical trials.

Professor Yongzhuo Huang

Shanghai Institute of Materia Medica
yzhuang@simm.ac.cn

Professor Yongzhuo Huang obtained his PhD from Zhejiang University and conducted postdoctoral training at the University of Michigan in Ann Arbor. He joined the Shanghai Institute of Materia Medica (CAS) in 2010 and was endorsed by CAS's prestigious 100 Talents Scholar

Program. His research interest is cancer-targeted drug delivery and tumour microenvironment modulation.

Targeting tumour-associated macrophage drug delivery and therapeutic strategy

Tumour microenvironments (TME) represent a complicated network of various tumour composites that suppress therapeutic responses and lead to drug resistance. The regulation of the immune subsets of TME could be helpful to remodel TME and achieve functional normalisation. For instance, tumour-associated macrophages (TAM) are abundant, representing the major population of innate immune cells at the TME and accounting for a portion—often up to 50%—of the tumour mass. The repolarisation of TAM from the protumor M2 subtype toward antitumor M1 can serve as a potent target for cancer therapy and overcome drug resistance.

In our research, we developed a two-birds-one-stone strategy for dual targeting delivery to TAM and cancer cells. Through dual action delivery on both the TAM and cancer cells, the TME can be remodelled and overcome the therapeutic resistance against chemotherapy drugs and molecular targeting drugs, as well as improve immunosuppression. Therefore, TAM-targeting delivery is a promising avenue for modulation of its anticancer functions.

Professor Jingya Li

Shanghai Institute of Materia Medica

jyli@simm.ac.cn

Professor Jingya Li is currently a principal investigator and professor in Shanghai Institute of Materia Medica (CAS), from which she obtained her PhD in pharmacology in 2003. As a scholar, Professor Li visited the Garvan Institute of Medical Research in 2006 and participated in the joint Sino-Australia research project. Afterwards, she initiated her research career at the National Center for Drug Screening, focusing on drug discovery of metabolic diseases. In the past ten years, Professor Li has published various papers in many top journals in metabolic disease field, such as Diabetes and Diabetologia and the Journal of Medicinal Chemistry. As a co-inventor of the drug candidate development, Professor Li has successfully obtained two candidates for ongoing pre-clinical evaluation for new molecular entities, with one candidate issued for clinical trials in China. Professor Li's research interests are mainly in pathological physiology, target validation and drug discovery for metabolic diseases.

STK17B facilitates islets β cells apoptosis and dysfunction by autophagy repression

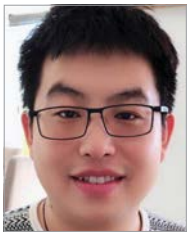
Islet β cells apoptosis is a detrimental event causing or aggravating type 2 diabetes (T2D). The attenuation of islet β cells is always accompanied by the development of T2D. Relieving islet β cells apoptosis and restoring its function are the fundamental strategies for treating diabetes. Serine/threonine-protein kinase 17B (STK17B), also called DAP-related apoptosis-inducing kinase-2 (Drak2), is a member of a death-associated protein kinase family. It has been reported that islets of Drak2 in transgenic mice are more susceptible to apoptosis. We found that the expression of Drak2 in the islets of diabetic monkeys, obese monkeys and diabetic mice were higher than those of normal individuals. We demonstrated that Drak2 activity was negatively related with glucose-stimulated insulin secretion and the autophagic flux.

To further investigate the role of Drak2 in islet function, we generated β cell specific Drak2 knockout mice (cKO) model. Drak2 cKO mice were resistant to high-fat diet induced metabolic syndrome; Drak2-deficiency protected β cells from PA-induced dysfunction. Mechanistically, Drak2 may be involved in autophagy regulation through autophagy initiation complex, ULK1, to exerting its effects on the function and apoptosis of islet cells. Our work showed that inhibition or deficiency of Drak2 protects β cell from apoptosis and suggests that Drak2 might be a potential target for diabetic therapeutics development.

Dr Xiang Li

University of Queensland

x.li12@uq.edu.au



Originally from Wuhan in China, Dr Xiang Li completed his Bachelor in Biotechnology from York University in Canada. Dr Li moved to Brisbane to work with Dr Timothy Bredy in 2010, and he received his PhD in neurosciences from the University of Queensland in 2016 for examining epigenetic changes on DNA on behavioural adaptation. In 2016, he started working with the University of California Irvine for his first postdoctoral training. In early 2017, Dr Li was awarded a UQ Development Fellowship for pursuing his postdoctoral training at the Queensland Brain Institute. Since then, his research has focused on how novel DNA modifications could regulate gene expression in the brain upon learning and memory formation. In 2019, Dr Li was awarded a prestigious Discovery Early Career Researcher Award from the Australian Research Council that allowed him to explore other epigenetic machinery in a rodent model that is associated with fear-related human mental diseases.

Elucidating the functional role of a novel DNA modification in response to fear-related memory formation

DNA modification is known to regulate experience-dependent gene expression. However, beyond cytosine methylation and its oxidated derivatives, very little is known about the functional importance of chemical modifications on other nucleobases in the brain. It was observed that in adult mice trained in fear extinction, the DNA modification N6-methyl-2'-deoxyadenosine (m6dA) accumulates, along with promoters and coding sequences in activated prefrontal cortical neurons. The deposition of m6dA is associated with increased genome-wide occupancy of the mammalian m6dA methyltransferase, N6amt1, and this correlates with extinction-induced gene expression. The accumulation of m6dA is associated with transcriptional activation at the brain-derived neurotrophic factor (Bdnf) P4 promoter, which is required for Bdnf exon IV messenger RNA expression and for the extinction of conditioned fear.

These results expand the scope of DNA modifications in the adult brain and highlight changes in m6dA as an epigenetic mechanism associated with activity-induced gene expression and the formation of fear extinction memory. The outcome of this research could increase our understanding of fear-related human mental diseases and provide novel drug targets and treatments for these diseases.

Dr Shafagh Waters

University of New South Wales

shafagh.waters@unsw.edu.au

Dr Shafagh Waters is a senior research associate at the School of Women's and Children's Health, and she heads the miCF Research Laboratory at the University of New South Wales in Sydney. Dr Waters received her PhD in RNA biology from the Australian National University and applies her skills to her current research activities that have a strong translational focus in three key areas:

- stem cell biology involving culture and biobanking of primary respiratory spheroids and rectal organoids from patients with cystic fibrosis
- prognostic and diagnostic exosomal biomarker discovery for CF related diabetes
- CFTR restoring therapeutics in patient-derived organoids using a variety of delivery approaches.

Towards personalised cystic fibrosis medicine: functional characterisation and targeted therapies for rare CFTR mutations using patient-derived organoids

Our research program aims to transform how we manage treatment of cystic fibrosis (CF) by advancing precision (genotype-specific) interventions for this common inherited monogenic disease. A novel class of targeted therapies that modulate CFTR—the protein that its considerable number (>2000) of mutations can lead to CF—have been discovered. The market authorisation of these therapies is granted to only half of the Australian CF population, as it is restricted to those with more common well-characterised CFTR mutations. The remaining 50% of the CF patients with rare, uncharacterised CFTR mutations have no access to life-changing targeted therapy. Despite some individuals with rare CFTR mutations showing benefit from the modulator therapy, the lifelong cost of $250 000 per patient per year makes their provision without evidence of efficacy economically unattainable, leading to significant inequality between patients.

To overcome the challenges associated with characterisation of over 2000 CFTR mutations, we integrate in silico molecular dynamics simulations with our personalised CFTR-drug screening in vitro platform (the miCF Avatar Platform). I will demonstrate the application of this platform by presenting comprehensive characterisation for two orphan CFTR mutations, I37R and R352Q. Each mutation is characterised using patient stem-cell derived mini-organs (organoids), molecular dynamic simulations, personalised CFTR functional assays and protein interatomics. The outcome of this research is a valuable biobank of CF patient organoids and improved understanding of the CFTR protein, ultimately matching patients with the best available current modulator therapy.

Dr Alex Wong

Centenary Institute

a.wong@centenary.org.au

Dr Alex Wong is a clinical haematologist with an interest in applying computational medicine to discover biomarkers in leukaemia and other cancers. He is completing his PhD at the Gene and Stem Cell Therapy Program at the Centenary Institute in Sydney, supervised by Dr Justin Wong and Professor John Rasko. His research investigates the role of intron retention in acute myeloid leukaemia, including modulation of key splicing factors and CRISPR-induced intron retention.

NxtIRF: discovering intron retention signatures in cancer

Intron retention, a form of alternative splicing that preserves specific non-coding intronic sequences in messenger RNA, acts as a 'brake' on gene expression in normal physiology and disease. Gene expression and other forms of alternative splicing have been explored as potential biomarkers to prognosticate and predict disease outcomes in cancer, but intron retention is relatively unexplored.

We introduce NxtIRF, an R statistical package and visualisation tool that facilitates intron retention biomarker discovery in cancer and other diseases. NxtIRF harnesses our previously published algorithm IRFinder to confidently measure intron retention as well as other forms of alternative splicing. User-friendly workflows streamline downstream publication-quality data visualisation, differential expression analysis, as well as survival analysis. Applying NxtIRF to the Cancer Genome Atlas datasets including acute myeloid leukaemia (n=133) and diffuse large B cell lymphoma (n=48), we discover distinct gene signatures associated with globally increased intron retention in multiple cancers, accompanied by impairment of nonsense-mediated decay pathways. Additionally, intron retention patterns predict disease outcomes in cancer alongside other forms of alternative splicing.

We conclude that NxtIRF streamlines analysis of intron retention in cancer and other diseases, facilitating biomarker discovery and characterisation.

Academy presidents

Professor Hugh Bradlow FTSE

Australian Academy of Technology and Engineering
hugh.bradlow@atse.org.au

Professor Hugh Bradlow FTSE is the current president of the Australian Academy of Technology and Engineering and an independent non-executive director of Silicon Quantum Computing Pty Ltd. He was previously the chief technology officer and head of innovation at Telstra, responsible for the research and development of new technologies and their introduction into Telstra's businesses. Subsequently, he became a chief scientist at Telstra, in which role he advised the Telstra board and management on the longer-term technology directions and technology disruption anticipated to impact Telstra and its customers. Before joining Telstra in September 1995, Professor Bradlow was a professor of computer engineering at the University of Wollongong and professor of electrical engineering (digital systems) at University of Cape Town.

Professor Bradlow graduated in electrical engineering from the University of Cape Town in 1973 and received his DPhil for research in experimental nuclear physics from the University of Oxford. He is an emeritus professor of the University of Wollongong, a professorial fellow of the University of Melbourne and recipient of a Centenary Medal from the Australian Government. He is globally recognised as a thought leader in telecommunications and was elected as the joint 2009 Australian Telecommunications Ambassador of the Year. He was also named by the Global Telecom Business as one of the 100 most influential telecommunications executives in the world and designated as one of the twelve most influential people in Australian ICT by Smart Company.

Professor John Shine AC PresAA

Australian Academy of Science
j.shine@garvan.org.au

Professor John Shine AC PresAA was executive director of the Garvan Institute of Medical Research from 1990 to 2011. He is a professor of molecular biology and professor of medicine at the University of New South Wales in Sydney. The 'father of gene cloning', Professor Shine was the first to clone human hormone genes and the first to sequence the replication of a cancer-causing virus. These and other pioneering discoveries by Professor Shine helped to launch the biotechnology revolution that has transformed medicine and agriculture. Professor Shine was appointed to the board of the biopharmaceutical company CSL Ltd in 2006 and as chair from 2011 to 2018. He received the Prime Minister's Prize for Science in 2010 and was elected a fellow of the Australian Academy of Science in 1994.

Academy staff

Ms Anna-Maria Arabia

Australian Academy of Science
annamaria.arabia@science.org.au

Ms Anna-Maria Arabia has over 20 years' experience in the science sector and is an experienced chief executive currently leading the Australian Academy of Science. In this role, Ms Arabia has led significant reform in global science engagement, in science policy matters and in addressing gender equity in science. Starting her career as a neuroscientist, Ms Arabia undertook medical research in Australia and abroad before applying her skills to policy development both in the Australian public service and in politics, where she has provided policy advice across many social and economic portfolios. She has held several senior executive positions in the science sector as CEO of Science and Technology Australia and deputy director at Questacon. Ms Arabia is a strategic and dispassionate advocate for science, social justice, diversity and inclusion.

Dr Margaret Hartley FTSE

Australian Academy of Technology and Engineering
margaret.hartley@applied.org.au

Dr Margaret Hartley FTSE is the chief executive officer at the Australian Academy of Technology and Engineering, leading the delivery of strategic policy and research activities to find solutions to technology challenges facing Australia. She works across a range of technology areas, including low carbon energy, industry innovation, agriculture, health technology and digital futures. She oversees the implementation of the Academy's diversity and inclusion strategy.

Formerly, Dr Hartley was with the Australian Government for 23 years in senior leadership and management roles, including as Australia's Chemical Regulator, as a director at the Office of Chemical Safety and as a principal science adviser at the Department of Health. She has led international collaboration projects with the Organisation for Economic Cooperation and Development, the World Health Organization and the Asia-Pacific Economic Cooperation, and has had held positions in biomedical research and public health.

Dr Carolyn O'Brien

Australian Academy of Technology and Engineering
carolyn.obrien@atse.org.au

Dr Carolyn O'Brien is the Senior International Relations Associate at the Australian Academy of Technology and Engineering, where she is responsible for the Academy's suite of international programs. She completed a PhD in political science at Monash University in 2002 and has worked as a researcher, curriculum developer and lecturer in political science programs at Monash University, Deakin University and the University of Melbourne.

In 2003 Dr O'Brien joined the International Relations Office at the University of Melbourne as an international policy advisor, where she focused on the development of global linkages for academic cooperation and exchange, and the provision of international education briefings and advice for the university's senior executive. In October 2015 she commenced in the international relations role with the Australian Academy of Technology and Engineering, which includes responsibility for the prestigious Australia-China Young Scientists Exchange Programme.

Ms Nancy Pritchard

Australian Academy of Science
nancy.pritchard@science.org.au

Ms Nancy Pritchard has worked at the Australian Academy of Science since 1992, initially in Academy's fundraising and science education areas. Since 2000 she has been in charge of the Academy's international activities. Ms Pritchard has worked closely with national academies of science and leading international partners to discuss science policy matters, facilitate scientific exchanges and coordinate international workshops and meetings to promote strategic partnerships between Australian and overseas researchers. In 2009, in recognition of her services to strengthen the bilateral cooperation with France, the French Government awarded her the Chevalier dans L'Ordre des Palmes Académiques. She served as secretary general to the Federation of Asian Scientific Academies and Societies from 2010 to 2013.

Ms Farhana Rahman

Australian Academy of Science
farhana.rahman@science.org.au

Ms Farhana Rahman is based in Canberra with the Australian Academy of Science, where she is responsible for coordinating events and programs that promote and engage Australian science globally. Ms Rahman obtained her master's degree in international relations from the Australian National University and has long experience fostering international linkages from working in the development and volunteer sectors and in diplomatic missions.

Ms Dongyao Wang

Chinese Academy of Sciences
dywang@cashq.ac.cn

Ms Dongyao Wang is the deputy director at the Office of American and Oceanian Affairs, Bureau of International Cooperation (CAS). Ms Wang has worked at the Office of European Affairs for the last nine years. She obtained her master's degree in science from the School of Chemistry at the University of Leeds in 2004. Ms Wang has rich experience in the promotion and coordination of international cooperation and partnerships in global science and engineering.

Mr Zhenyu Wang

Chinese Academy of Sciences
dywang@cashq.ac.cn

Mr Zhenyu Wang has been the deputy director-general at the Bureau of International Cooperation (CAS) since May 2019. Mr Wang graduated from Beijing Foreign Studies University with a Diploma in International Politics and Relations in 1995. Afterwards he worked in the Bureau of International Cooperation as a program officer and later as a deputy and division director in charge of the cooperative programs with Europe and international organisations. From 1998 to 1999, Mr Wang worked at the University of London as an assistant professor.

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