

**PROGRAM**

15-16 OCTOBER 2015

MELBOURNE,

AUSTRALIA

# Australia–China symposium *on* neuroscience



Australian Government



Australian Academy of Science



Australian Academy of Technological  
Sciences and Engineering (ATSE)

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The flower icon used in this program was inspired by the ink and wash painting *Flower in jar* by Chinese artist Bada Shanren (1626–1705)

# Welcome



The Australian Academy of Science, the Australian Academy of Technological Sciences and Engineering (ATSE), and the Chinese Academy of Sciences have held annual symposia since 2004, alternating between sites in China and Australia. Each symposium focused on a topic of great importance to both countries, such as energy, food security, astronomy and biotechnology. These meetings have provided opportunities to build strong bilateral networks and increase international research collaborations between China and Australia.

The Australian Academies are pleased to welcome the delegation from the Chinese Academy of Sciences that will participate in the Australia–China Symposium on Neuroscience in Melbourne on 15–16 October 2015. The Chinese researchers will be led by Professor Jinghai Li, Vice-President of the Chinese Academy of Sciences. Professor Li has strong links to Australia, including as a Foreign Fellow of ATSE, and we salute his continued involvement and support for the joint Academies' symposia.

Researchers who are working towards new treatments for neurodegenerative diseases and mental illnesses rely on better methods to study brain function and development. At the symposium, Chinese and Australian researchers will discuss their research on major brain disorders, epilepsy, mental health and dementia, and the complexities of brain circuitry.

We are delighted that a feature of the 2015 symposium is the participation of early- and mid-career researchers from both countries as well as senior Chinese-Australian researchers who know the Chinese and Australian research and innovation systems well and who will act as a bridge between researchers from both countries.

The Australian Academies are delighted to be hosting this meeting and wish to thank the Australian Government departments of Education and Training and Industry, Innovation and Science, as well as the Chinese Academy of Sciences, for their continued support. We also wish to acknowledge the strong support of the Chinese Embassy in Canberra.

Diseases of the brain are health and societal challenges common to both countries. There is considerable potential for China and Australia to cooperate and provide regional and international leadership, researching innovative responses to these challenges. The conclusions of the participants and our Academies, Chinese and Australian, will provide a platform for enhancing collaboration between the two countries through innovative scientific, technological and engineering solutions.

**Professor Andrew Holmes** AM PresAA FRS FTSE  
President  
Australian Academy of Science

**Dr Alan Finkel** AO FTSE  
President  
Australian Academy of Technological  
Sciences and Engineering

# Program

## THURSDAY, 15 OCTOBER 2015

0900–0915	<b>Welcome and opening of symposium</b> Professor Andrew Holmes President, Australian Academy of Science
<b>Session 1: Brain circuitry</b>	
0915–0945	<b>Keynote presentation</b> <i>The future of medical science: using new technologies to reduce the risk of mental illness and suicide in young people</i> Associate Professor Jane Burns Young and Well Cooperative Research Centre
0945–1010	<i>Wiring the developing brain</i> Professor Linda Richards Queensland Brain Institute, University of Queensland
1010–1035	<i>Face processing in the human occipitotemporal cortex</i> Professor Sheng He Institute of Biophysics, Chinese Academy of Sciences
1035–1100	<b>MORNING TEA</b>
1100–1125	<i>SK channels and spike timing-dependent synaptic plasticity</i> Professor Greg Stuart Eccles Institute of Neuroscience, Australian National University
1125–1150	<i>Molecular and synaptic bases of paroxysmal kinesigenic dyskinesia</i> Dr Zhi-Qi Xiong Institute of Neuroscience, Chinese Academy of Sciences
1150–1235	<b>Session 1 round table and wrap-up</b>
1235–1335	<b>LUNCH</b>
<b>Session 2: Major brain disease/disorder</b>	
1335–1405	<b>Keynote presentation</b> <i>Where to with the China Brain Project?</i> Professor Mu-Ming Poo Institute of Neuroscience, Chinese Academy of Sciences
1405–1430	<i>Scientific insights into epilepsy genetics transform clinical practice</i> Professor Ingrid Scheffer University of Melbourne; Florey Institute of Neuroscience and Mental Health
1430–1455	<i>Lipids in neural development and disease</i> Professor Yong Zhang Institute of Genetics and Developmental Biology, Chinese Academy of Sciences
1455–1520	<b>AFTERNOON TEA</b>
1520–1545	<i>Direct and emergent phenotypes in genetic epilepsy: implications for precision therapeutics</i> Professor Steven Petrou Florey Institute of Neuroscience and Mental Health
1545–1610	<i>MEKK3 coordinates with FBW7 to regulate microcephaly associated protein WDR62 and neurogenesis</i> Professor Zhiheng Xu Institute of Genetics and Developmental Biology, Chinese Academy of Sciences
1610–1655	<b>Session 2 round table and wrap-up</b>
1800–1930	<b>Cocktail reception and early- and mid-career researcher poster presentations</b>
1930–2200	<b>Official symposium dinner</b>

## FRIDAY, 16 OCTOBER 2015

<b>Session 3: Major brain disease/disorder (continued)</b>	
0835–0905	<b>Keynote presentation</b> <i>Functional genomics approaches to human neurological diseases</i> Professor Ernst Wolvetang Australian Institute for Bioengineering and Nanotechnology, University of Queensland
0905–0930	<i>A<math>\beta</math> is the critical target for preclinical, prodromal and clinical Alzheimer's disease modifying therapy</i> Professor Colin Masters University of Melbourne; Florey Institute of Neuroscience and Mental Health
0930–0955	<i>Hypothalamic CRF-controlling multiple paired receptors imbalance in the pathogenesis of depression</i> Professor Jiang-Ning Zhou University of Science and Technology of China
0955–1020	<b>MORNING TEA</b>
1020–1045	<i>Regulating neurogenic precursors in the hippocampus may reverse cognitive impairment in aged animals</i> Professor Perry Bartlett Queensland Brain Institute, University of Queensland
1045–1110	<i>Reverse translational study for developing novel drugs and understanding disease mechanisms</i> Professor Lin Xu Kunming Institute of Zoology, Chinese Academy of Sciences
1110–1155	<b>Session 3 round table and wrap-up</b>
1155–1255	<b>LUNCH</b>
<b>Session 4: Big Brain Project (genomics, imaging, biostatistics)</b>	
1255–1325	<b>Keynote presentation</b> <i>Defining the primitives of visual cognition: the global-first topological definition of perceptual objects</i> Professor Lin Chen Institute of Biophysics, Chinese Academy of Sciences
1325–1350	<i>Gene discovery for human complex traits and diseases: SNP array or whole-genome sequencing?</i> Associate Professor Jian Yang Queensland Brain Institute, University of Queensland
1350–1415	<i>Brainnetome atlas: a new brain atlas based on connectivity profiles</i> Professor Tianzi Jiang Brainnetome Center, Institute of Automation, Chinese Academy of Sciences
1415–1440	<b>AFTERNOON TEA</b>
1440–1505	<i>Large-scale brain imaging genomic projects</i> Associate Professor Margie Wright Queensland Brain Institute, University of Queensland
1505–1530	<i>Development of virus-based tools for neurocircuit tracing</i> Professor Fuqiang Xu Wuhan Institute of Physics and Mathematics, Chinese Academy of Sciences
1530–1615	<b>Session 4 round table and wrap-up</b>
1615–1630	<b>Symposium wrap-up and farewell</b> Professor Peter Gray Vice-President, Australian Academy of Technological Sciences and Engineering
1630	Transport from the Mansion Hotel and Spa at Werribee Park to Melbourne Airport and CBD



# Speakers

## PROFESSOR PERRY BARTLETT

**Foundation Professor of Molecular Neuroscience**  
**Queensland Brain Institute**  
**University of Queensland**  
**Email: p.bartlett@uq.edu.au**



Professor Perry Bartlett was inaugural Director of the Queensland Brain Institute and is a professor of molecular neuroscience. Previously he was Head of the Division of Development and Neurobiology at the Walter and Eliza Hall Institute of Medical Research. He has been responsible for a series of groundbreaking

discoveries in neuroscience, which have often overturned existing dogma and led to a new understanding, particularly in the areas of neuronal precursor regulation and neuron survival in the developing and adult nervous system. Most prominent among these was his laboratory's discovery in 1992 of the presence of stem cells in the adult brain that had the capacity to produce new neurons. His group was the first to isolate and characterise these stem cells in 2001 and more recently revealed the presence of a latent hippocampal stem cell population that influences learning and memory.

Professor Bartlett is a Fellow of the Australian Academy of Science (FAA), a past NHMRC Senior Principal Research Fellow and Australian Research Council Federation Fellow and a past president of the Australian Neuroscience Society. He has championed interactions with China, establishing three joint neuroscience laboratories, two with the Chinese Academy of Sciences.

### ***Regulating neurogenic precursors in the hippocampus may reverse cognitive impairment in aged animals***

The production of new neurons in the hippocampus of adult mice, shown to be important for regulating some forms of learning and memory, decreases substantially as the animals age, with little or none in animals over 18 months. Coincident with this decrease is the significant impairment to spatial learning suffered by the aged animals, suggesting the two may be linked.

In 2008, we discovered the presence of a quiescent population of neurogenic precursors even in the very old animals and began investigating their molecular regulation in order to determine its effects on learning and memory. Exercise is known to increase hippocampal neurogenesis in younger animals, and our recent studies have revealed that aged animals require a different, but precise, length of exercise for activation to occur. Only animals who run for this precise period show a significant recovery in spatial learning, almost to the level of young controls. Moreover, we show that ablating the production of the new neurons

following precursor activation completely ablates this recovery, indicating that the effect is mediated by this mechanism. We have defined some of the molecular regulators mediating this improvement and believe they may have future application in ageing humans with cognitive decline.

## ASSOCIATE PROFESSOR JANE BURNS

**Founder and Chief Executive Officer**  
**Young and Well Cooperative Research Centre**  
**Email: jane@yawcrc.org.au**



Jane Burns is the founder and Chief Executive Officer of the Young and Well Cooperative Research Centre, an organisation that unites young people with researchers, practitioners and innovators to explore the role of technology in improving mental health and wellbeing for young people aged

12 to 25. Jane holds a Principal Research Fellowship at Orygen, the National Centre of Excellence in Youth Mental Health, and an Honorary Fellowship at the Brain and Mind Research Institute. She has led the youth agenda for beyondblue, was a Commonwealth Fund Harkness Fellow at the University of California, San Francisco, and was Director of International Partnerships at Inspire Foundation. Jane held a VicHealth fellowship from 2006–2013, an NHMRC fellowship from 1997 to 2000 and an NHMRC scholarship from 1994 to 1996. She holds a PhD in medicine from the Faculty of Medicine (Public Health and Epidemiology), University of Adelaide. Associate Professor Burns was a winner in the category of Innovation for 2015's Australian Financial Review and Westpac Group 100 Women of Influence, and was a Victorian Finalist in the 2012 Telstra Business Women's Awards. She is a graduate of the Australian Institute of Company Directors.

### ***The future of medical science: using new technologies to reduce the risk of mental illness and suicide in young people***

While there are many differences between towns in Australia and villages in China, one commonality is that most young people have mobile phones, are internet literate and are connected to social media. We have real opportunities to disrupt medical science for positive outcomes in the future; technology has the potential to redefine medical research. Australia leads the world in the use of e-health platforms to promote wellbeing and improve mental health service delivery, though the full expression of e-health possibilities is yet to be realised. Up to 80 per cent of young people are not seeking help for mental health difficulties due to factors including isolation, stigma and complicated funding models. Providing online support has the benefit of being less expensive than face-to-face care but,

ultimately, the real mental health care revolution can happen when we see an integration of these two modes of service delivery—creating more well-rounded, continual, wider-reaching provision of services, resulting in increased positive mental health outcomes. Exploration of opportunities for international collaboration in this field would help to reduce the burden of mental illness in young people in both China and Australia.

## PROFESSOR LIN CHEN

Professor

Institute of Biophysics

Chinese Academy of Sciences

Email: [linchen@bcslab.ibp.ac.cn](mailto:linchen@bcslab.ibp.ac.cn)



Professor Lin Chen is Director of the Beijing MRI Center for Brain Research, Institute of Biophysics, Chinese Academy of Sciences. His research effort focuses on visual cognition and brain mapping. He is an elected member of the Chinese Academy of Sciences and The World Academy of Sciences.

### *Defining the primitives of visual cognition: the global-first topological definition of perceptual objects*

What is a perceptual object over which visual cognition operates? The global-first topological approach proposes that the core intuitive notion of a perceptual object—the holistic identity preserved over shape-changing transformations—may be characterised formally as topological invariants, such as connectivity and holes, and the topological change may lead to the emergence of a new object. This global-first topological definition has been tested with experimental data collected at different levels of cognition, including perceptual organisation, motion, attention, numerosity perception, emotion and consciousness, in normal adult human subjects as well as in infants, patients, honey bees and zebrafish. The results demonstrate that the extraction of topological properties serves as the starting point of object representation, and the topological change is indeed perceived as an emergence of a new object, while object identity may survive various non-topological changes. The functional magnetic resonance imaging (fMRI) experiments further showed that the topological changes activated the anterior temporal lobe and amygdala.

## PROFESSOR SHENG HE

Investigator

Institute of Biophysics

Chinese Academy of Sciences

Email: [shenghemn@gmail.com](mailto:shenghemn@gmail.com)



Professor Sheng He received his Bachelor of Science in biophysics from the University of Science and Technology of China in 1986 and his PhD in psychology from the University of California, San Diego, in 1995. After two years of postdoctoral training at Harvard University, he took a faculty position at

the University of Minnesota in 1997 and became a professor in 2007. He is currently Director of the State Key Laboratory of Brain and Cognitive Sciences at the Institute of Biophysics, Chinese Academy of Sciences. He is broadly interested in the neural basis of human vision, visual attention and visual awareness. He uses psychophysical, functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) approaches in his research. His main contributions to cognitive neuroscience include the demonstration, using different forms of invisible visual patterns, of extensive cortical information processing in the absence of visual awareness.

### *Face processing in the human occipitotemporal cortex*

The human occipitotemporal cortex features a number of areas sensitive to faces, but its functional properties and relative contributions to face processing remain unclear. We identified a dozen robust face-sensitive regions in the occipitotemporal cortex, and systemically investigated their face sensitivity and selectivity using a large set of images. Data were analysed based on both regionally averaged activation levels and multi-voxel activation patterns. Results show that these regions differ in degrees of face-category selectivity and face-exemplar sensitivity. The bilateral posterior Fusiform Face Areas (pFFAs) had the highest and most robust face categorisation ability, together with the right Occipital Face Area (rOFA), constituting the core system for face processing. The bilateral posterior Superior Temporal Sulcus (pSTS) and Anterior Face Patch (AFP) are most distinct from other face-sensitive regions, and likely play key roles in identifying individual faces. In a related study of blind participants, we investigated the genesis of the face selectivity of the Fusiform Face Areas (FFAs). Results suggest a strong genetic basis as well as the critical need for early face exposure for the development of FFAs' face selectivity.

## PROFESSOR TIANZI JIANG

Professor and Director  
Brainnetome Center, Institute of Automation  
Chinese Academy of Sciences  
Email: [jiangtz@nlpr.ia.ac.cn](mailto:jiangtz@nlpr.ia.ac.cn)



Tianzi Jiang is Professor and Director of the Beijing Key Laboratory of Brainnetome and Director of the Brainnetome Center, Institute of Automation, at the Chinese Academy of Sciences. He is the core member of the Chinese Academy of Sciences Center for Excellence in Brain Science and

Intelligence Technology, and Professor at the Queensland Brain Institute, University of Queensland. His research interests include neuroimaging, brainnetome and imaging genetics, and their clinical applications in brain disorders. He is the author or co-author of over 200 reviewed journal papers in these fields and the coeditor of six issues of the *Lecture notes in computer science*. He is Associate Editor of *IEEE Transactions on Autonomous Mental Development* and *Neuroscience Bulletin*, and Section Editor of *BMC Neuroscience*.

### **Brainnetome atlas: a new brain atlas based on connectivity profiles**

Brain atlases are the fundamental tools for both basic and clinical neuroscience. However, existing atlases lack finer grained parcellation results and do not provide important connectivity information. This lecture presents a new brain atlas—the *Brainnetome atlas*. It is constructed with brain connectivity profiles. The *Brainnetome atlas* is in vivo, with finer grained brain subregions, and with anatomical and functional connection profiles. This talk will give a brief introduction to the history of the development of the brain atlas followed by an exposition of the basic ideas in the atlas and the procedure by which it is constructed. Some parcellation results of representative brain areas will be presented. There will also be a brief presentation on how to use the atlas to address issues in neuroscience and clinical research—for example, in determining the boundary of Wernicke's area, the organisation of Broca's area across languages or the mechanism of visuospatial attention lateralisation, as well as for new findings in basic and clinical neuroscience.

## PROFESSOR COLIN MASTERS

Professor  
University of Melbourne  
Florey Institute of Neuroscience and Mental Health  
Email: [c.masters@unimelb.edu.au](mailto:c.masters@unimelb.edu.au)



Colin Masters' career has focused on research into Alzheimer's disease (AD) and other neurodegenerative diseases, including Creutzfeldt-Jakob disease. His work over the last 35 years is widely acknowledged as having had a major influence on Alzheimer's disease research worldwide, particularly the collaborative

studies conducted with Konrad Beyreuther in which they discovered the proteolytic neuronal origin of the A $\beta$  amyloid protein which causes Alzheimer's disease. This work has led to the continued development of diagnostics and therapeutic strategies. More recently, his focus has been on describing the natural history of Alzheimer's disease as a necessary preparatory step for therapeutic disease modification.

### **A $\beta$ is the critical target for preclinical, prodromal and clinical Alzheimer's disease modifying therapy**

There are two basic forms of Alzheimer's disease. The common (more than 95 per cent) form is sporadic, and is caused by the failure to clear the A $\beta$  peptide (mean age at onset 80 years). The rare (less than 5 per cent) autosomal dominant familial form is caused by the overproduction of this peptide (mean age at onset 45 years). In both forms, the kinetics of A $\beta$  accumulation are similar, taking about 30 years to accumulate approximately 10 milligrams of A $\beta$ . Thus we estimate that sporadic AD starts at about the age of 50 years and the autosomal dominant form starts at about 15 years of age. A disease-modifying strategy will be needed to keep the total brain A $\beta$  burden close to normal levels (less than 2.5 milligrams) and prevent or delay onset of both forms. Such a strategy may encompass lowering production, stabilising or neutralising the toxic A $\beta$  species, and promoting its clearance from the brain. Interventions targeting A $\beta$  in the earliest or mildest stages of the natural history of AD are beginning to show efficacies.

## PROFESSOR STEVEN PETROU

Deputy Director and Division Head  
Florey Institute of Neuroscience and Mental Health  
Email: [spetrou@unimelb.edu.au](mailto:spetrou@unimelb.edu.au)



Professor Petrou is a neuroscientist focused on understanding disease mechanisms in genetic epilepsy. He has made seminal contributions to our understanding of the mechanisms underlying the pathology of genetic epilepsy. His pioneering disease models have identified the pathological changes

that precede epilepsy, showing that early treatment is critical for controlling seizures and the attendant quality-of-life-destroying comorbidities. His recent work is the first to show that disease mechanism-based therapies can be effective treatments in epilepsy, paving the way for future precision therapeutics benefiting millions of patients and their families.

### *Direct and emergent phenotypes in genetic epilepsy: implications for precision therapeutics*

In the decades after the initiation of the Human Genome Project, the idea that treatments could be targeted to genetically defined subgroups of individuals has often been proposed but rarely realised. The advent of next-generation sequencing has promoted a new wave of enthusiasm embodied in the catchphrase 'precision medicine'. Precision medicine refers to the scientific basis that underpins the personalisation of medical care, particularly in the context of treatments targeted towards the precise molecular causes of disease. The realisation of precision medicine is perhaps best illustrated in the specialty of cancer, in which mechanism-based treatments have successfully moved from bench to bedside. A deep understanding of the genetic and molecular underpinnings of epilepsy reveals not only the direct impacts of disease-causing mutations but also unexpected emergent pathology that presents multiple opportunities for targeted therapy.

## PROFESSOR MU-MING POO

Director  
Institute of Neuroscience  
Chinese Academy of Sciences  
Email: [mpoo@ion.ac.cn](mailto:mpoo@ion.ac.cn)



Mu-Ming Poo received a Bachelor of Science in physics from Tsing Hua University, Taiwan, in 1970 and a PhD in biophysics from Johns Hopkins University in 1974. He has served on the faculty of the University of California (Irvine, San Diego and Berkeley), and at Yale and Columbia universities. He has been

Director of the Institute of Neuroscience, Chinese Academy of Sciences, since 1999 and is currently also Director of the Chinese Academy of Science's Center for Excellence in Brain Science and

Intelligence Technology. Poo received the Ameritex Prize in 2001, the China International Science and Technology Cooperation Award in 2005 and the Qiushi Distinguished Scientist Award in 2011. He was awarded an honorary doctorate by the Ecole Normale Supérieure (Paris) and Hong Kong University of Science and Technology. He is a member of Academia Sinica (Taiwan) and the National Academy of Sciences (USA) and a foreign member of the Chinese Academy of Sciences. His research interests include nerve growth, synaptic plasticity and neural circuit functions.

### *Where to with the China Brain Project?*

The past two years have been marked by a wave of global awareness about the urgency of brain research, as reflected by projects initiated in Europe, the United States and Japan. Discussions among Chinese neuroscientists in several strategic meetings organised by the Ministry of Science and Technology have led to the consensus that understanding the neural basis of cognitive processes remains a universal goal of neuroscience and should form the central pillar of the China Brain Project.

In addition, there is general agreement that China should also devote its resources and unique research capabilities to addressing immediate social needs, particularly the development of preventive, diagnostic and therapeutic approaches for major brain diseases. Given the importance of brain-inspired computation methods and devices, there should also be organised programs to foster in-depth collaboration between neuroscientists and information technologists, with a focus on understanding how the highly efficient processing, storage and retrieval of multimodal information is achieved by the brain and could be simulated by artificial neural networks and devices. This talk will summarise China's strengths and weaknesses in these areas, and give perspectives on the potential contribution of the China Brain Project to the global drive in brain research.

## PROFESSOR LINDA RICHARDS

Laboratory Head and Deputy Director, Research  
Queensland Brain Institute  
University of Queensland  
Email: [richards@uq.edu.au](mailto:richards@uq.edu.au)



Professor Richards is a developmental neurobiologist who completed her Bachelor of Science (Honours) and PhD at the Walter and Eliza Hall Institute of Medical Research, Melbourne, and postdoctoral training at the Salk Institute for Biological Studies, California. Professor Richards established her independent

laboratory focused on understanding the developmental mechanisms regulating the formation of the corpus callosum at the University of Maryland School of Medicine, Baltimore, in 1997. In 2005, she moved her research program to the Queensland Brain Institute at the University of Queensland where she is currently an NHMRC principal research fellow and



is Laboratory Head and Deputy Director, Research. She has been awarded the CJ Herrick Award by the American Association of Anatomists (2004), the Nina Kondelos Prize by the Australasian Neuroscience Society (2011) and the University of Queensland's Equity and Diversity Award (2013). In 2015, she was elected Fellow of the Australian Academy of Science and is currently President-elect of the Australasian Neuroscience Society.

### **Wiring the developing brain**

The correct wiring of the brain is essential for function. Researchers at the laboratory of the Queensland Brain Institute investigate the important genetic, molecular and cellular mechanisms regulating the development of brain wiring, and how changes in brain wiring affect brain function throughout life. They study the corpus callosum which connects the two cerebral hemispheres, and have identified important mechanisms regulating axonal crossing of the cerebral midline. Human subjects with corpus callosum agenesis/dysgenesis are currently identified based on their structural midline phenotype, a limit imposed by current clinical neuroimaging capabilities. However, these subjects are likely to represent subgroups with more severe forms of callosal dysgenesis. More subtle changes in callosal targeting could represent a much larger and diverse group of subjects that have normal midline crossing, but disrupted targeting in the contralateral hemisphere. This area of research is in its formative stages but could offer potentially major breakthroughs in how the brain is normally wired during development and what mechanisms may be disrupted in disorders of brain connectivity.

Acknowledgement of funding: National Health and Medical Research Council, Australia, the Australian Research Council, and the National Institutes of Health, USA. Professor Richards is supported by an NHMRC Principal Research Fellowship.

### **PROFESSOR INGRID SCHEFFER**

**Professor of Paediatric Neurology**

**University of Melbourne**

**Florey Institute of Neuroscience and Mental Health**

**Email: [scheffer@unimelb.edu.au](mailto:scheffer@unimelb.edu.au)**



Professor Ingrid Scheffer is a physician-scientist whose work as a paediatric neurologist at the University of Melbourne and Florey Institute has led the field of epilepsy genetics over 20 years, with Professor Samuel Berkovic and molecular geneticists. This resulted in identification of the first epilepsy gene

and many genes subsequently. Professor Scheffer has described many novel epilepsy syndromes and genotype-phenotype correlation. She recently led the first reclassification of the epilepsies in two decades as Chair of the International League Against Epilepsy Commission for Classification. Her awards include the American Epilepsy Society Clinical Research Award and the L'Oréal-UNESCO Women in Science Laureate for the

Asia-Pacific region. In 2014, she was elected a Fellow of the Australian Academy of Science and inaugural Vice-President of the Australian Academy of Health and Medical Sciences. Professor Scheffer was awarded the Order of Australia and, together with Professor Berkovic, the Prime Minister's Prize for Science.

### **Scientific insights into epilepsy genetics transform clinical practice**

Epilepsy is a central nervous system disorder in which seizures arise due to aberrant neuronal firing and dysfunctional networks. The unpredictable and varied nature of seizures makes epilepsy a challenging disorder with which to live. In children with severe epilepsies beginning in infancy or childhood, epilepsy is often accompanied by serious comorbidities such as autism spectrum disorders, intellectual disability and an increased mortality risk. Focal epilepsies where seizures begin in one region of the brain were considered acquired disorders until relatively recently.

Our initial discovery of a nicotinic receptor as the first epilepsy gene and the cause of autosomal dominant nocturnal frontal lobe epilepsy suggested that epilepsies were channelopathies. Then followed the advent of the molecular revolution which led to major insights into the aetiologies of the epilepsies, informing our understanding of their neurobiology. Many of the severe epilepsies with infantile onset have recently been shown to be due to de novo dominant mutations with marked genetic heterogeneity. Gene discovery is the key to understanding the molecular pathways involved, often resulting in convergence on specific processes. Most exciting is the paradigm shift to precision medicine using mutation discovery to plan functional studies and explore novel targeted therapies.

### **PROFESSOR GREG STUART**

**Head**

**Eccles Institute of Neuroscience**

**Australian National University**

**Email: [greg.stuart@anu.edu.au](mailto:greg.stuart@anu.edu.au)**



Greg Stuart is currently Professor and Head of the Eccles Institute of Neuroscience at the John Curtin School of Medical Research at the Australian National University, Canberra. He completed his undergraduate studies at Monash University, majoring in physiology, before going on to do

a PhD in neuroscience at the Australian National University. He is considered a world expert on neuronal dendrites and has pioneered methods that have allowed neuroscientists to probe the function of nerve cells at unprecedented resolution. He has received a number of national and international fellowships and awards, and was recently appointed to the Australian Academy of Science in recognition of his seminal contributions to understanding how information is processed by individual nerve cells within the brain.

## **SK channels and spike timing-dependent synaptic plasticity**

This talk will describe how action potentials (APs) propagating into the dendritic tree modulate excitatory postsynaptic potentials (EPSPs) in pyramidal neurons by activating small conductance calcium-activated potassium channels (SK channels) in dendritic spines. SK channels activated by backpropagating APs suppressed EPSPs in both cortical and hippocampal pyramidal neurons in a time-dependent manner. This effect was dendritic as it was absent during somatic EPSPs and persisted during block of somatic SK channels. Furthermore, EPSP suppression was dependent on N-methyl-D-aspartate (NMDA) receptor activation. Finally, SK channel activation by APs gates STDP induction during single AP-EPSP pairing, with both long-term potentiation (LTP) and long-term depression (LTD) absent under control conditions but present after SK channel block. These findings resolve a number of previous observations and indicate that activation of SK channels in spines during APs plays a key role in regulating both EPSP amplitude and STDP induction.

## **PROFESSOR ERNST WOLVETANG**

**Group Leader**

**Australian Institute for Bioengineering and Nanotechnology  
University of Queensland**

**Email: e.wolvetang@uq.edu.au**



Professor Wolvetang obtained his PhD from the University of Amsterdam. After investigating the role of chromosome 21 transcription factors in Down syndrome during his postdoctoral studies, he joined the laboratory of Professor Martin Pera to help pioneer human embryonic stem cell research. In 2009, he took up a group

leader position at the Australian Institute for Bioengineering and Nanotechnology at the University of Queensland to interface with emerging microfluidic, nano- and 'smart' surface technologies at the institute. His laboratory employs induced pluripotent stem cells (iPSC) as in-vitro disease models and uses clustered regularly interspaced short palindromic repeats (CRISPR) genome-editing tools to interrogate the underlying gene regulatory networks and epigenetic bases of, in particular, complex neurological diseases. He leads Cell Reprogramming Australia, won the 2014 Life Sciences Queensland Regenerative Medicine Award and is a principal investigator in the Australian Research Council Centre of Excellence 'Stem Cells Australia'.

## **Functional genomics approaches to human neurological diseases**

Induced pluripotent stem cells capture an individual's genetic make-up and, following differentiation into cell types of the brain, provide an attractive model system to perform functional genomics investigations into human brain diseases. While in-vitro co-culture of different human brain cell types in 2D and 3D culture formats do not, and perhaps never can, match the

complexity of the in-vivo brain, they can provide novel insights into human neurological conditions, help elucidate the underlying gene regulatory pathways and permit facile drug screening. This talk examines the generation of iPSC from patients with mutant Aspartate-tRNA synthetase (DARS), which causes hypomyelination with brain stem involvement and leg spasticity, and CRISPR engineered patient mutations into control iPSC to reveal disease phenotypes and perform drug screening. It looks at the use of CRISPR/Cas9 editing technology in iPSC to investigate genotype-phenotype relationships between the supernumerary chromosome 21 genes in Down syndrome and trisomy 21 phenotypes, such as early onset Alzheimer's disease and neural crest pathologies.

## **ASSOCIATE PROFESSOR MARGIE WRIGHT**

**Principal Research Fellow, Group Leader, Human Cognitive Ageing and Imaging Genomics**

**Queensland Brain Institute**

**University of Queensland**

**Email: margie.wright@uq.edu.au**



Associate Professor Margie Wright is Head of the Human Cognitive Ageing and Imaging Genomics group at the Queensland Brain Institute and the Centre for Advanced Imaging, University of Queensland. Her research focuses on the neurobiological causes and modifiers of normal cognitive function, especially

brain disorders, using neuroimaging, neuropsychological tests, and behavioural and molecular genetic approaches. She is recognised internationally for pioneering the collection of multimodal imaging from large population samples, together with behavioural and genetic data, initiating the Queensland Twin Imaging Study, one of the first large-scale magnetic resonance imaging (MRI) studies in twins in the world. She also directs the Queensland arm of the Older Australian Twins Study, a multi-site study of healthy brain ageing, which is being extended to a middle-age cohort, and is a founding member of the Enhancing Neuro Imaging Genetics through Meta Analysis (ENIGMA) consortium, a worldwide effort using genome-wide association meta-analysis to identify genetic variants that affect the brain.

## **Large-scale brain imaging genomic projects**

To understand how disorders inflict the brain over the lifespan, the complexities of the normal brain must first be understood. With the initiation of large-scale MRI studies in twins, and analysis of imaging and genetic data on a new scale, we now know that there is a strong genetic influence (heritability) on brain structure, and overlap of genetic effects (pleiotropy) between structures, and between structure and cognition—though there is also evidence for genetic specificity, with distinct genetic effects across some brain regions. In order to have sufficient power to identify these genetic variants, and to take advantage of the scale that consortium approaches can bring, the ENIGMA

consortium was founded. While the primary aim of ENIGMA is to conduct large-scale genome-wide association study (GWAS) meta-analyses of imaging phenotypes, this effort has expanded to include prospective meta-analyses of imaging phenotypes to identify how mental illnesses affect the brain. Currently a network of researchers in ENIGMA are working on large-scale studies that integrate imaging data from over 24,000 subjects and over 70 institutions worldwide. The current progress of these big brain projects, along with challenges and unexpected discoveries made on the way, will be reviewed.

## DR ZHI-QI XIONG

**Principal Investigator**  
**Institute of Neuroscience**  
**Chinese Academy of Sciences**  
**Email: xiongzhiqi@ion.ac.cn**



Dr Zhi-Qi Xiong received his bachelor's degree in pharmacy in 1992 from West China University of Medical Sciences (Sichuan University), his master's degree in 1995 from the Shanghai Institute of Materia Medica, Chinese Academy of Sciences, and his PhD in 2000 from Baylor College of Medicine, Texas.

He was a postdoctoral research associate in the laboratory of Dr James O McNamara at Duke University Medical Center from 2000 to 2003. He is currently an investigator and Head of the Laboratory of Neurobiology of Disease at the Institute of Neuroscience, Chinese Academy of Sciences. Research in Dr Xiong's laboratory aims to understand the molecular and synaptic bases of neurodevelopmental disorders.

### **Molecular and synaptic bases of paroxysmal kinesigenic dyskinesia**

Paroxysmal kinesigenic dyskinesia (PKD) is an episodic disorder characterised by attacks of involuntary movement following sudden movements. Individuals are typically normal between attacks. The attacks in PKD consist of dystonic posturing, chorea or athetosis movements. Onset is typically during childhood or adolescence and may remit in adulthood. Diagnostic criteria for PKD include attacks with an identified kinesigenic trigger and of short duration (usually less than one minute), without alteration of consciousness or pain during attacks. The disorder was often familial and therefore a genetic cause was proposed. In 2011, mutations in the gene PRRT2 encoding proline-rich transmembrane protein 2 were successfully identified in eight Chinese families with PKD. This finding was rapidly followed by many reports of mutations in the same gene in patients from different ethnic backgrounds with PKD, benign familial infantile convulsions, or infantile convulsions with choreoathetosis. Over 95 per cent of PRRT2 mutations reported so far are truncating mutations predicted to lead to haploinsufficiency. We have successfully generated PRRT2 mutant and conditional knockout

mice and established a genetic model of PKD that is overtly symptomatic. This talk will examine the molecular and synaptic bases for how PRRT2 deficiency selectively disrupts neural circuits and leads to movement disorder.

## PROFESSOR FUQIANG XU

**Professor**  
**Wuhan Institute of Physics and Mathematics**  
**Chinese Academy of Sciences**  
**Email: fuqiang.xu@wipm.ac.cn**



Fuqiang Xu obtained PhDs in chemistry and in physiology from the University of Kentucky in 1994 and 1998 respectively. After his postdoctoral training at Yale, he joined the Yale Magnetic Resonance Research Center in 2001. In 2007, he moved to the Wuhan Institute of Physics and Mathematics, Chinese Academy of

Sciences, as an endowed professor, and won the Outstanding Young Scientist Award. Today, he is also a core member of the Center for Excellence in Brain Science and Intelligence Technology at the Chinese Academy of Sciences, and Adjunct Professor at Wuhan National Laboratory of Optoelectronics and SIAT-McGovern (MIT) Joint Institute of Brain Cognition and Diseases. His research in the past several years has mainly been on the development of tools to reveal the structures and functions of neurocircuits, through integrating neurobiology, neuroimage, neuroscience, virology, genetics, and molecular and cellular biology. He has published about 40 papers in journals including *Science*, *Trends in Neurosciences*, *Nature Communications*, *PNAS*, the *Journal of Neuroscience* and *NeuroImage*.

### **Development of virus-based tools for neurocircuit tracing**

All our brain functions, such as basic condition-controlling, learning and decision-making, are based on corresponding neural circuits and, accordingly, 'mental illness is defined as disruption in neural circuits' (National Institute of Mental Health, 2011). For a complete elucidation of the mechanisms of a given brain function, we must know the exact structures of all circuits related to that precise function. However, the studies at circuit level on both structures and functions have been hindered by a lack of effective tools. In the past seven years, the group has been developing tools to trace the neuronal circuits and to apply them to reveal the detailed structures of neuronal connections. By using molecular, genetic and cellular methods to modify and construct viral tools, over a hundred viral tracing systems have been successfully established and used in several dozens of laboratories and hospitals for a variety of purposes in non-human primates, rats, mice and zebrafish. This talk will give a brief update of the laboratory's progress in the relevant areas.

## PROFESSOR LIN XU

Principal Investigator  
Kunming Institute of Zoology  
Chinese Academy of Sciences  
Email: lxxu@vip.163.com



Professor Lin Xu received a Bachelor of Science in 1985 from Nanchong Normal University, a Master of Science in 1990 from Kunming Institute of Zoology, Chinese Academy of Sciences, and a PhD in 1998 from Trinity College, Dublin. He is Professor of Neuroscience at the Kunming Institute of Zoology, Chinese Academy of

Sciences. Using the rodent and treeshrew models of depression, addiction, post-traumatic stress disorder (PTSD) and Alzheimer's disease, pharmacological tools, positron emission tomography/computed tomography (PET/CT), optogenetic and virus tracing techniques, microelectrode array and field excitatory postsynaptic potential (fEPSP) recordings in freely moving animals, Professor Xu's laboratory is trying to address how memory is stored and retrieved by the hippocampus, and how abnormality of memory mechanisms contributes to neuropsychiatric disorders and Alzheimer's disease. He has published over 100 research articles, including in *Nature*, *Cell*, *Neuron*, *PNAS* and the *JNS*. Professor Xu has also developed two novel drugs, KMBZ009 and CXZ123, for the treatment of Alzheimer's disease and depression respectively, both of which are under clinical trial phase II in China.

### Reverse translational study for developing novel drugs and understanding disease mechanisms

Years of research into major depressive disorder, Alzheimer's disease, drug addiction and ischemic stroke have yielded significant results. Nevertheless, these achievements are rarely translated into effective clinical treatments—for example, over 100 clinical trials of new drugs for treating Alzheimer's disease and ischemic stroke failed. In contrast, reverse translational studies are greatly successful. Traditional Chinese herbs have long been used for treating diseases—that is, there is evidence for their clinical efficacy. For over 1,000 years, *Curculigo orchoides Gaertn.*, featured in traditional Chinese medicine, has been credited with improving mind power and memory. Our laboratory found that Orcinoside, a small compound derived from this herb, produced antidepressant effects and enhanced memory through a glutamatergic mechanism. This may be consistent with the finding that ketamine produces rapid onset of antidepressant action through glutamate receptors. However, Orcinoside differs from ketamine in that it is safer and enhances memory. The laboratory has demonstrated that reverse translational study would be an excellent strategy for developing novel drugs and understanding possible disease mechanisms.

## PROFESSOR ZHIHENG XU

Principal Investigator  
Institute of Genetics and Developmental Biology  
Chinese Academy of Sciences  
Email: zhxu@genetics.ac.cn



Dr Zhiheng Xu is Principal Investigator at the Institute of Genetics and Developmental Biology, Chinese Academy of Sciences. He was awarded an MD in 1989 from the Second Military Medical University, Shanghai, and a PhD in 1999 from Rutgers University, New Jersey. In 1999 he was a postdoctoral and

research associate at Columbia University, New York. He received the Ruth L Kirschstein National Research Service Award in 2003 and the Distinguished Young Investigator Award, National Science Foundation (China), in 2007.

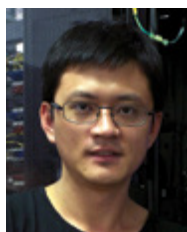
### MEKK3 coordinates with FBW7 to regulate microcephaly associated protein WDR62 and neurogenesis

Human autosomal recessive primary microcephaly (MCPH) is a neural developmental disorder hallmarked by reduced brain size and intellectual disability. Mutation of WD40-repeat protein 62 (WDR62) is the second major cause of MCPH. We have demonstrated that WDR62 regulates the maintenance of neural progenitor cells (NPCs) during cortical development through JNK1. However, the detailed biological function of WDR62 and the underlying mechanism by which WDR62 regulates JNK signalling are still not clear. This talk will demonstrate that MEKK3 forms a complex with WDR62 to promote JNK signalling synergistically and regulate neurogenesis as well as brain size. MEKK3, WDR62 and JNK1 depletion or knockout phenocopy each other in defects including premature NPC differentiation and reduced brain size. These defects can be rescued by the expression of transgenic JNK1, indicating that the complex controls neurogenesis through JNK signalling. It will be shown that WDR62 protein level is positively regulated by MEKK3 through JNK1-induced WDR62 phosphorylation. Meanwhile, WDR62 is also negatively regulated by specific phosphorylation of WDR62 at T1053, leading to the recruitment of the E3 ligase FBW7 and proteasomal degradation of WDR62. Our findings demonstrate that WDR62 controls the maintenance of NPCs via MEKK3 and JNK1 during cortical development and reveal the molecular mechanisms underlying MCPH pathogenesis.



## ASSOCIATE PROFESSOR JIAN YANG

Principal Research Fellow  
Queensland Brain Institute  
University of Queensland  
Email: jian.yang@uq.edu.au



Jian Yang is Principal Research Fellow at the Queensland Brain Institute, the University of Queensland. He received his PhD in 2008 from Zhejiang University, China, which was followed by postdoctoral research at the Queensland Institute of Medical Research. He joined the University of Queensland in 2012. His

research interests are in developing novel methods and software tools to better understand the genetic architecture of complex diseases and traits using high-throughput genetic and genomic data. In 2012, he won the Centenary Institute Lawrence Creative Prize, which is awarded annually to only one young medical researcher in Australia. He received an NHMRC RD Wright Career Development Fellowship in the same year, and was part of a team shortlisted for the Eureka Prize in Scientific Research. He was one of two recipients of the Sylvia and Charles Viertel Charitable Foundation's Senior Medical Research Fellowship in 2013, and was awarded the Australian Academy of Science Ruth Stephens Gani Medal for distinguished research in human genetics in 2015.

### Gene discovery for human complex traits and diseases: SNP array or whole-genome sequencing?

Most human complex traits (e.g. height and cognition) and diseases (e.g. obesity and schizophrenia) are influenced by a large number of genes each with a small effect. It has been extremely difficult to identify genes for complex traits (including diseases) in humans until the application of the genome-wide association study (GWAS) technology in large samples. GWAS has identified thousands of genetic loci associated with hundreds of complex traits in humans. For most traits, however, the GWAS loci only explained a small proportion of heritability, that is, the so-called missing heritability problem. The choice of experimental designs for gene discovery in the future depends on the quantification of the relative contributions of common and rare genetic variants to complex trait variation. We propose a method (GREML-LDMS) to estimate heritability for human complex traits in unrelated individuals using whole-genome sequencing data. We demonstrate that ~97 per cent and ~68 per cent of variation at common and rare variants, respectively, can be captured by SNP array followed by imputation. Therefore, for further discovery of genes associated with complex traits, a study design with SNP arrays followed by imputation is more cost effective than whole-genome sequencing at current prices.

## PROFESSOR YONG ZHANG

Deputy Director  
Institute of Genetics and Developmental Biology  
Chinese Academy of Sciences  
Email: yqzhang@genetics.ac.cn



Yong Zhang is Professor at the Institute of Genetics and Developmental Biology, Chinese Academy of Sciences. He received his PhD from China Agricultural University and undertook postdoctoral training first in genetics at Cambridge University and then in neurobiology at the University of Utah and Vanderbilt

University. He is currently an associate editor of *Journal of Genetics and Genomics*, Editor-in-Chief of *Hereditas*, an editor of *Scientific Reports*, and a faculty member in genetics and genomics of Faculty of 1000. His laboratory uses *Drosophila melanogaster* as a primary model system and focuses on unravelling novel mechanisms underlying synapse development and functions in physiological and pathological conditions using an interdisciplinary approach including genetics, biochemistry, electrophysiology, live imaging and behavioral assays.

### Lipids in neural development and disease

Lipids are major components of cellular membranes and play a fundamental role in living organisms. Mutations in lipid biosynthetic enzymes result in various neurological and psychiatric disorders. However, how lipids affect neural development remains poorly understood, partly because of the complexity of lipid structures and associated synthetic and metabolic pathways. From a genetic screen, we unravel that mannosyl glucosylceramide (MacCer), a species of glycosphingolipids, is a positive regulator of synapse formation at the *Drosophila* neuromuscular junctions (NMJs). Tissue-specific loss- and gain-of-function studies of Egghead (Egh) and Brainiac (Brn), which are involved in the synthesis and conversion of MacCer, reveal that MacCer promotes NMJ growth in the presynaptic neurons. In addition, disruption of lipid rafts by depleting sphingolipids or sterols results in reduced NMJ growth. Furthermore, MacCer positively regulates the synaptic level of Wingless/Wnt1 (Wg), a raft-associated protein, thereby affecting the local presynaptic activity of Wg signalling and synaptic growth. These findings uncover a novel mechanism whereby the specific GSL MacCer promotes synapse formation via local lipid raft-mediated Wg signalling.

## PROFESSOR JIANG-NING ZHOU

Professor

University of Science and Technology of China

Email: [jnzhou@ustc.edu.cn](mailto:jnzhou@ustc.edu.cn)



Jiang-Ning Zhou received his PhD in Neurobiology from the University of Amsterdam, The Netherlands. From 1979 to 1992 he was a lecturer and Associate Professor of Physiology at Ningxia Medical University. Since 1998 Professor Zhou has been Professor of Neurobiology at the University of Science and Technology of China.

### *Hypothalamic CRF-controlling multiple paired receptors imbalance in the pathogenesis of depression*

Hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis is one of the most consistent biological findings in major depression. As the activity-initiating factor, the corticotropin-

releasing factor (CRF) neurons in the paraventricular nucleus (PVN) of the hypothalamus play a key role in determining the state of the HPA axis. We showed that a number of receptors co-localise with CRF neurons in human PVN, regulating the transcription and expression of CRF. Imbalance of three pairs of CRF-regulating receptors is involved in the pathogenesis of depression: CRF receptor 1 (CRFR1)/CRF receptor 2 (CRFR2), mineralocorticoid receptor (MR)/glucocorticoid receptor (GR) and estrogen receptor (ER)/androgen receptor (AR). The imbalance of multiple paired receptors in regulating the activity of CRF neurons indicates possible molecular network mechanisms underlying depression aetiology and directs novel therapeutic strategies for depression in the future.

# Roundtable participants

## PROFESSOR SILVIU ITESCU

Chief Executive Officer

Mesoblast Limited

Email: [Silviu.Itescu@mesoblast.com](mailto:Silviu.Itescu@mesoblast.com)



Silviu Itescu has served on Mesoblast's board of directors since the company's founding in 2004, was Executive Director from 2007, and became Chief Executive Officer and Managing Director in 2011. Prior to founding Mesoblast in 2004, Professor Itescu established an international reputation as a physician

scientist in the fields of stem cell biology, autoimmune diseases, organ transplantation and heart failure. He has been a faculty member of Columbia University in New York, and of Melbourne and Monash universities in Australia. In 2011, Professor Itescu was named BioSpectrum Asia Person of the Year. In 2013, he received the inaugural Key Innovator Award from the Vatican's Pontifical Council for Culture for his leadership in translational science and clinical medicine in relation to adult stem cell therapy. Professor Itescu has consulted for various international pharmaceutical companies, has been an adviser to biotechnology and health care investor groups, and has served on the boards of directors of several publicly listed life sciences companies.

## DR JOHN PARKER

Chief Executive Officer

Saluda Medical

Email: [john.parker@saludamedical.com](mailto:john.parker@saludamedical.com)



John Parker is CEO of Saluda Medical Pty Ltd, an Australian-based company working to commercialise feedback controlled neuromodulation technology. He has an academic background (PhD, Australian National University) and has worked in both Australian and international universities. He has authored

numerous scientific publications and patents. Dr Parker joined Cochlear Ltd in 1994 and was appointed an executive director of the company in 2002. During a 13-year career at Cochlear, Dr Parker served in a number of senior management functions including COO and Head of R&D and CTO before leaving Cochlear to join NICTA in 2007. Dr Parker is an ATSE Fellow, Harvard Business School (PMD) graduate, docent at the Royal Institute of Technology in Stockholm, Sweden, ATSE Clunies Ross Medallist (2010) and adjunct professor at the UNSW School of Biomedical Engineering. He is an experienced director of both listed and non-listed companies and cooperative research centres.

# Experts

## PROFESSOR MAX LU

**Provost and Senior Vice-President  
University of Queensland  
Email: provost@uq.edu.au**



Max Lu is Provost and Senior Vice-President at the University of Queensland. He had previously served as Deputy Vice-Chancellor (Research) and Pro-Vice-Chancellor (Research Linkages) from 2008 to 2014. He was Foundation Director of the ARC Centre of Excellence for Functional Nanomaterials from 2003

to 2009. His areas of expertise are in nanomaterials for energy and environmental applications, with more than 33,000 citations and an h-index of 90. He is a Thomson Reuters Highly Cited Researcher in both chemistry and materials science. He won the prestigious ARC Federation Fellowship in 2003 and 2008. Professor Lu has served on numerous government committees and advisory groups including those under the Prime Minister's Science, Engineering and Innovation Council and ARC College of Experts. He has won many awards, such as the Chemeca Medal, China International Science and Technology Award, and a Queensland Great. He is a Fellow of the Australian Academy of Science, IChemE, and the Australian Academy of Technological Sciences and Engineering.

## PROFESSOR AIBING YU

**Vice-Chancellor's Professorial Fellow  
Monash University**

**Pro Vice-Chancellor and President  
Southeast University–Monash University Joint Graduate  
School (Suzhou)  
Email: Aibing.Yu@monash.edu**



Aibing Yu is Vice-Chancellor's Professorial Fellow, Pro Vice-Chancellor and President of Monash–Southeast University Joint Research Institute, Monash University, after 22 years with the University of NSW (UNSW). He was inaugural Director of the UNSW Centre for Simulation and Modelling of Particulate Systems, Deputy Director of

ARC Centre of Excellence for Functional Nanomaterials, Founding Director of the Australia–China Joint Research Centre for Minerals, Metallurgy and Materials, and ARC Research Hub for Computational Particle Technology. He is also the chair of the Technical Advisory Committee of the Baosteel–Australia Joint Research and Development Centre. Professor Yu has received numerous prestigious awards including the UNSW Scientia Professorship, ARC Federation Fellowship, NSW Scientist of the Year, and the Australian Academy of Science's Ian Wark Medal and Lecture. He is a Fellow of the Australian Academy of Science and the Australian Academy of Technological Sciences and Engineering.



# Early- and mid-career researchers

## PROFESSOR PENG CAO

Professor

Institute of Biophysics

Chinese Academy of Sciences

Email: caopeng1978@hotmail.com



Peng Cao received his BSc in 2000 at Peking University and his PhD in 2005 at the Chinese Academy of Sciences, where he is a professor of neurobiology at the Institute of Biophysics. He is also a member of the Chinese Academy of Sciences' Center for Excellence in Biomacromolecules. His primary research

interests are the synaptic and circuit mechanisms underlying brain function and disorders. He has published a dozen original research articles in *Science*, *Cell*, *Nature Neuroscience*, *PNAS* and the *Journal of Neuroscience*. His recent work identified novel synaptic and circuit mechanisms underlying innate (visually guided fight-or-flight response) and learned (olfactory social learning) behaviours in the mammalian brain.

**Poster title: Synaptotagmin-1 and -10 in the olfactory bulb synergistically control social learning in mice**

Synaptotagmins (Syts) function as major calcium sensors for exocytosis. It is not yet known how distinct forms of exocytosis mediated by different synaptotagmins are synchronised to control synaptic function and associated behaviors. We found that Syt1- and Syt10-dependent vesicle exocytosis pathways coexisted in the same synapse of the olfactory bulb neurons *in vivo*. During social learning, Syt1 gated synaptic transmission by mediating calcium-triggered synaptic vesicle exocytosis. Syt10 controlled a social learning-induced long-term synaptic potentiation between granule and mitral cells by triggering activity-dependent exocytosis of neurotrophic factor IGF-1. Deletion of Syt1 and Syt10 in the olfactory bulb of adult mice disrupted the formation and maintenance of socially acquired food preference, respectively. Therefore, parallel synaptotagmin-dependent vesicle exocytosis pathways in mouse olfactory bulb neurons were synchronised by social learning to mediate synaptic transmission and plasticity, and thereby the initiation and stabilisation of socially acquired behavior.

## DR VINCENT DORÉ

Research Scientist

CSIRO

Email: vincent.dore@csiro.au



Vincent Doré completed a PhD in image process in 2009 at the University of Quebec in Canada. He joined the Australian e-Health Research Centre (CSIRO) in 2010. Since 2012, Dr Doré has been based in the nuclear department of Austin Hospital, Melbourne, collaborating with clinicians on the

Australian Imaging, Biomarker and Lifestyle (AIBL) study. His current interests are in providing clinicians with automatic and robust tools to extract relevant biological information from positron emission tomography (PET) and MRI images, especially in the context of Alzheimer's disease (AD). He recently developed a novel method for surface-projection of PET images from all radiotracers without the need for an MRI. This new technology is currently being evaluated at Austin Hospital as a clinical inspection tool for AD and other neurodegenerative conditions. This technology has also recently been extended to new tau PET tracers and the evaluation of these novel tracers is envisioned.

**Poster title: Automated reporting of Amyloid PET quantification on brain surface through a web interface**

Molecular brain imaging using PET is a robust diagnostic tool for which several tracers labelled with either <sup>11</sup>C or <sup>18</sup>F are available. For visual inspection of the images, cortical surface based visualisation presents the advantage of providing a compact and more convenient display than volumetric scans. We have developed an automated reporting tool that performs quantitative PET measurements without the need for an MRI. It provides clinical researchers with convenient, reliable and objective PET image analysis. CAPAIBL (Computational Analysis of PET from AIBL) automatically aligns, segments and measures PET signals which are then compared to healthy populations. This tool estimates the PET signal in the brain cortex and displays the result on a standard brain surface with units of SUVR and Z-score. This reduces subjectivity and brings quantified measurements of FDG, Amyloid and tau straight to the user. The method was validated by comparing the surface signal computed with and without MRI.

Visual inspection revealed high concordance between PET-only and MRI-based surface projection; the surface projection was defined on eight standard views for consistent reporting. Across the six tracers tested, the average absolute error over the brain surface with and without MRI was 0.12SUVR, whereas the average variance was 0.018SUVR. The proposed MRI-less surface projection method demonstrated better estimation of <sup>11</sup>C-PIB

retention than recently published methods displaying similar accuracy for various 18F labelled radiotracers. CAPAIBL provides an efficient reporting tool for PET imaging easily accessed remotely through a web interface.

## DR ZHITAO HU

**Group Leader**

**Queensland Brain Institute**

**University of Queensland**

**Email: uqzhu4@uq.edu.au**



Zhitao Hu was appointed as a faculty member and currently runs his own independent laboratory in the Queensland Brain Institute at the University of Queensland. He is working on the neuroscience study by using *C. elegans* as an excellent genetic model. His career goal is to understand the molecular

mechanisms of synaptic transmission and the function of neural circuits. The neurotransmitters are released from the presynaptic terminal and activate the receptors on the postsynaptic plasma membrane. The 'communication' between synapses is essential to the normal functioning of the nervous system, and is related to an individual's cognition and behavior. Combining electrophysiological recording, cellular imaging, molecular biology and biochemistry approaches, Dr Hu is currently focusing on four lines of research: kinetics regulation of synaptic vesicle release; molecular/cellular mechanism of different release forms; synaptic transmission defect of neurological diseases; and neural circuit function regulating behavior and cognition.

### **Poster title: UNC-13L, UNC-13S, and Tomosyn form a protein code for fast and slow neurotransmitter release in *Caenorhabditis elegans***

Synaptic transmission consists of fast and slow components of neurotransmitter release. Here we show that these components are mediated by distinct exocytic proteins. The *Caenorhabditis elegans* unc-13 gene is required for SV exocytosis, and encodes long and short isoforms (UNC-13L and S). Fast release was mediated by UNC-13L, whereas slow release required both UNC-13 proteins and was inhibited by Tomosyn. The spatial location of each protein correlated with its effect. Proteins adjacent to the dense projection mediated fast release, while those controlling slow release were more distal or diffuse. Two UNC-13L domains accelerated release. C2A, which binds RIM (a protein associated with calcium channels), anchored UNC-13 at active zones and shortened the latency of release. A calmodulin binding site accelerated release but had little effect on UNC-13's spatial localisation. These results suggest that UNC-13L, UNC-13S and Tomosyn form a molecular code that dictates the timing of neurotransmitter release.

## PROFESSOR HONGXING LEI

**Professor**

**Beijing Institute of Genomics**

**Chinese Academy of Sciences**

**Email: leihx@big.ac.cn**



Hongxing Lei received his PhD from Kansas State University in 2003 and is a professor of computational systems biology at Beijing Institute of Genomics, Chinese Academy of Sciences. He is also an adjunct professor at Beijing Institute for Brain Disorders. Professor Lei has been working in the field of bioinformatics and

computational biology since 1991. His past works include the first sub-angstrom folding of a native protein and simulations of amyloid peptide aggregation. Since 2008, Professor Lei has shifted his focus to the understanding of Alzheimer's disease (AD) from the whole-genome perspective. His research covers many aspects of AD including the genetic risk, disease mechanism and non-invasive biomarkers. He is also trying to incorporate stem cell technology into his research on AD. The information from genome-scale investigations of AD has been curated by his group into an online public resource named AlzBase.

### **Poster title: Gene hunting in Alzheimer's woods**

Alzheimer's disease is the most prevailing form of senile dementia. The pathological hallmarks of AD include extracellular deposition of A $\beta$  amyloid plaques and intra-neuronal tangles composed of hyper-phosphorylated tau. The advent of genomics technologies has made it possible to go beyond A $\beta$  and tau and take a holistic look at the transformation of neural cells. Valuable information regarding AD pathogenesis may come from transcriptome studies of AD brains. In the past few years, we have been attempting to dissect the gene network in AD mainly based on publicly available brain transcriptome data. Through this work, we have proposed the down-regulation of genes in energy metabolism in early AD as an adaptive strategy. We have identified a hub gene network in multiple brain regions. We have also found that chromosome 19p is the most actively dysregulated genomic region during AD pathogenesis. Through meta-analysis of brain transcriptome data, we have ranked the dysregulated genes and proposed several critical genes. In addition, we have also discovered several potential risk genes for AD in our reanalysis of multiple GWAS datasets. Our work on the peripheral blood of AD has also suggested potential non-invasive biomarkers for AD.

## DR PENG LEI

Senior Research Officer

Florey Institute of Neuroscience and Mental Health

Email: peng.lei@florey.edu.au



Dr Peng Lei is a senior research officer at the Florey Institute of Neuroscience and Mental Health, University of Melbourne. He is the recipient of several awards including the Chancellor's Prize for Excellence in a PhD Thesis from the University of Melbourne (PhD awarded 2012), a commendation in the Victorian

Premier's Award for Health and Medical Research 2014 and an Early Career Fellowship from the NHMRC. Dr Lei has authored 25 publications (with 682 citations since 2010) and two patents. He has been invited to speak at both local and major international conferences 10 times. Since 2008, he has been frequently asked by high-ranking journals for his reviews and opinions. His work on the function of tau protein recast the importance of this protein in health, and was featured in national and international academic journals and news networks. Currently he focuses on the physiological functions of tau protein.

### **Poster title: Tau-mediated APP trafficking contributes to neurodegeneration by regulating iron export**

Iron accumulation was found in both Alzheimer's disease (AD) and Parkinson's disease (PD). Until recently, we discovered  $\beta$ -amyloid protein precursor (APP) facilitates the efflux of iron from the cell via its transport to the cell surface where it interacts with the iron exporter, ferroportin. Deletion of tau decreases mature APP on the cell surface, causing an iron export lesion that resulted in an age-dependent neuronal iron accumulation paralleling studies with APP deficient cell cultures and brain tissue. In tau KO mice, we found an age-dependent Parkinsonism with dementia phenotype which was prevented by oral treatment with a moderate iron chelator, clioquinol. Coincident with iron elevation, both nigral tau and APP levels were decreased in both human cases and in the mouse PD MPTP model. Collectively, these data indicate a new relationship between two characteristic proteins related to AD and show how disruption in either or both functions can lead to pro-oxidant neuronal Fe<sup>2+</sup> elevation and contribute to neurodegenerative diseases such as AD and PD.

## DR EDWIN LIM

Senior Research Fellow

Macquarie University

Email: edwin.lim@mq.edu.au



Edwin Lim obtained his PhD in pharmacology from the University of New South Wales in 2011. Since then, he has developed an interest in understanding how tryptophan metabolism is involved in the link between neuroinflammation and neurodegeneration using models

of Alzheimer's disease, multiple sclerosis, and psychiatric disorders such as schizophrenia, depression and autism spectrum disorder. Recently he has extended his interests to tryptophan metabolomics affecting physiological functions such as protein synthesis, mood, sleep, immune and energy (NAD) regulation. His research currently focuses on understanding how changes to tryptophan metabolism in response to proinflammation can affect those physiological functions during disease progression. This has significant implications for biomarker discovery and devising personalised therapeutic options.

### **Poster title: Tryptophan metabolism in autism spectrum disorder: implications for novel therapeutic regimes**

Our study provides the first conclusive evidence linking the alteration of the kynurenine pathway (KP) of tryptophan metabolism to autistic spectrum disorder. Using state-of-the-art analytical technology, we overturn previous studies that failed to identify this correlation. Furthermore, our data provide a rational explanation of the alterations in serotonergic and glutamatergic neurotransmission found in autism, linking these changes to both immune activation and defects in the 16p11.2 chromosome.

Our study demonstrates the first comprehensive evaluation of the KP metabolic profile in a cohort of autistic children in comparison with age-matched healthy controls. This consequently led to increased production of downstream KP metabolite quinolinic acid, which is an NMDA agonist that can enhance glutamatergic neurotransmission.

Increased quinolinic acid may be explained by 16p11.2 mutation observed in autism, responsible for encoding the catabolic enzyme of quinolinic acid known as quinolinate phosphoribosyltransferase. Our data also correlate with immune markers suggesting changes to the KP metabolism may be immune driven.

By highlighting the roles of the immune system and tryptophan metabolism dysfunction in autism, our study supports the development of new therapeutic strategies via KP modulation in autistic spectrum disorders.

## DR YEN YING LIM

Research Fellow

Florey Institute of Neuroscience and Mental Health

Email: [yen.lim@florey.edu.au](mailto:yen.lim@florey.edu.au)



Yen Ying Lim is currently a research fellow at the Florey Institute of Neuroscience and Mental Health, University of Melbourne. She is heavily involved in cognition cores of the Australian Imaging, Biomarkers and Lifestyle (AIBL) study, and the Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU). Her

research has focused on the assessment of cognitive change in dementia, the relationship between biological, genetic and cognitive markers in the very early stages of dementia, and the translation of these results for secondary prevention clinical trials of Alzheimer's disease. She has a keen interest in understanding whether environmental or genetic factors may affect cognitive decline in the very early stages of Alzheimer's disease.

### **Poster title: Effect of BDNF Val66Met on preclinical Alzheimer's disease**

Brain-derived neurotrophic factor (BDNF) Val66Met polymorphism has previously been implicated in Alzheimer's disease (AD)-related cognitive impairment. We aimed to determine whether BDNF Val66Met moderates A $\beta$ -related cognitive decline, reduction in hippocampal volume, and A $\beta$  accumulation in healthy older adults. Healthy older adults (n=165) enrolled in the Australian Imaging, Biomarkers and Lifestyle study underwent PiB-PET neuroimaging for A $\beta$ , BDNF genotyping, and cognitive assessment at baseline, 18 and 36 months. Linear mixed models determined rates of change in cognition, hippocampal volume and A $\beta$  accumulation over 36 months.

In A $\beta$ + healthy older adults, Met carriers showed significant and moderate-to-large decline in episodic memory, executive function and language, and greater reductions in hippocampal volume over 36 months compared to Val/Val homozygotes. BDNF Val66Met was unrelated to rates of change in cognition or hippocampal volume in A $\beta$ - participants. BDNF was not associated with levels of A $\beta$  in A $\beta$ - or A $\beta$ + participants at baseline. Similarly, BDNF was not associated with rates of A $\beta$  accumulation in A $\beta$ - or A $\beta$ + participants. BDNF Val66Met moderated the association between A $\beta$ + and cognitive decline and hippocampal atrophy in healthy older adults. A $\beta$ + coupled with Met carriage may be useful prognostic markers of accelerated cognitive decline and hippocampal degeneration in individuals in preclinical AD.

## DR MALINDA TANTIRIGAMA

Postdoctoral Fellow

Australian National University

Email: [malinda.tantirigama@anu.edu.au](mailto:malinda.tantirigama@anu.edu.au)



Malinda Tantirigama received his PhD from the University of Otago, New Zealand, in 2013. He is currently a postdoctoral fellow at the Australian National University in Canberra investigating how circuits of the primary olfactory cortex encode odour information. The piriform cortex

is thought to assemble 'odour images' from fragmented chemical information, and its relatively simple anatomy makes it an ideal brain region to study how the brain works. He aims to decode the circuit activity using electrophysiology and 2-photon calcium imaging techniques in an in vivo mouse experimental preparation.

### **Poster title: Dynamics of spontaneous activity in the mouse piriform cortex in vivo**

The mammalian brain remains highly active independent of external input. Spontaneous activity carries important information about a network's baseline state, and so its dynamics should reveal features of the network's function. In this project we studied the origin and statistical properties of spontaneous activity in the piriform cortex (PC) by simultaneously measuring the activity of up to 255 neurons in the PC of anaesthetised mice using 2-photon microscopy and functional calcium imaging. We found that the kinetics and frequency of spontaneous calcium transients differed significantly between the two main types of principal cells in the PC. For both cell types, the frequency distribution deviated from a Poisson distribution, indicating a non-random temporal structure in the spontaneous events. Application of the NMDA channel blocker MK801 to the PC completely abolished spontaneous activity, indicating a strong dependence on NMDA receptor-driven neurotransmission. To test whether spontaneous activity is associated with activity in the olfactory bulb (OB), we removed the ipsilateral OB and found that the occurrence of spontaneous activity was significantly reduced, and removal of OBs in both hemispheres abolished all activity in the PC. The findings suggest that computations in the PC are superimposed on cell type-specific non-random spontaneous activity that emerges from the OB.



## DR LACHLAN THOMPSON

Principal Research Fellow

Florey Institute of Neuroscience and Mental Health

Email: lachlan.thompson@florey.edu.au



Lachlan Thompson received his PhD in neuropharmacology at Monash University in 2002 before undertaking a five-year postdoctoral period at Lund University in Sweden, where he studied under Professor Anders Björklund in the area of neural transplantation. In 2008 he returned to Australia to continue research

in this area and is currently Head of the Neurogenesis and Neural Transplantation laboratory and Principal Research Fellow at the Florey Institute. A key focus of the laboratory is to understand the capacity of neurons generated from pluripotent stem cells to functionally integrate after transplantation to replace damaged brain circuitry, particularly in models of Parkinson's disease and stroke.

### **Poster title: In vivo properties of neurons generated from human pluripotent stem cells**

Human pluripotent stem cells have the capacity for directed differentiation into a wide variety of neuronal subtypes that may be useful for brain repair. While a substantial body of research has led to a detailed understanding of the ability of neurons in foetal tissue grafts to structurally and functionally integrate after intra-cerebral transplantation, we are only just beginning to understand the in-vivo properties of neurons derived from human pluripotent stem cells. Here we have utilised the human embryonic stem (ES) cell line Envy, which constitutively expresses green fluorescent protein (GFP), in order to study the in-vivo properties of neurons derived from human ES cells. Rapid and efficient neural induction, followed by differentiation as neurospheres, resulted in a GFP+ neural precursor population with traits of neuroepithelial and dorsal forebrain identity. Ten weeks after transplantation into neonatal rats, GFP+ fibre patterns revealed extensive axonal growth in the host brain, particularly along host white matter tracts, although innervation of adjacent nuclei was limited. The grafts were composed of a mix of neural cell types including differentiated neurons and glia, but also dividing neural progenitors and migrating neuroblasts, indicating an incomplete state of maturation at 10 weeks. This was reflected in patch-clamp recordings showing stereotypical properties appropriate for mature functional neurons, including the ability to generate action potentials, as well as profiles consistent for more immature neurons. These findings illustrate the intrinsic capacity for neurons derived from human ES cells to integrate at a structural and functional level following transplantation.

## PROFESSOR LIPING WANG

Professor

Shenzhen Institutes of Advanced Technology

Chinese Academy of Sciences

Email: lpwang@siat.ac.cn



Liping Wang received his PhD from the Charité – Universitätsmedizin, Berlin, Germany in 2005. Since then he has held the position of Postdoctoral Fellow at the California Institute for Regenerative Medicine and is currently Professor and Director at the Shenzhen Key Lab of Neuropsychiatric Modulation, Brain

Cognition and Brain Disease Institute (BCBDI), Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences.

### **Poster title: Processing of visually evoked innate fear response by a non-canonical thalamic pathway**

The ability of animals to respond to life-threatening stimuli is essential for survival. Although vision provides one of the major sensory inputs for detecting threats across animal species, the circuitry underlying defensive responses to visual stimuli remains poorly defined. Here, we investigate the circuitry underlying innate defensive behaviors elicited by predator-like visual stimuli in mice. Our results demonstrate that neurons in the superior colliculus (SC) are essential for a variety of acute and persistent defensive responses to overhead looming stimuli. Optogenetic mapping revealed that SC projections to the lateral posterior nucleus (LP) of the thalamus, a non-canonical polymodal sensory relay, are sufficient to mimic visually evoked fear responses. In-vivo electrophysiology experiments identified a di-synaptic circuit from SC through LP to the lateral amygdala, and lesions of the amygdala blocked the full range of visually evoked defensive responses. Our results reveal a novel collicular-thalamic-amygdala circuit important for innate defensive responses to visual threats.

## PROFESSOR XIAOQUN WANG

Professor

Institute of Biophysics

Chinese Academy of Sciences

Email: xiaoqunwang@ibp.ac.cn



Xiaoqun Wang received his PhD with Honours from the Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, in 2004. Since that time his major research experience has been in the USA where he was Visiting Scholar at the Department of Biopharmaceutical Sciences, University

of California, San Francisco, from 2004 to 2006. Dr Wang then took up a position as Research Fellow in the Developmental

Biology program at the Memorial Sloan Kettering Cancer Centre (MSKCC) in New York. From 2010 to 2012, Dr Wang was Assistant Professor (Research) at the Department of Neurology and Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research, University of California, San Francisco. He is now a professor at the Institute of Biophysics, Chinese Academy of Sciences.

**Poster title: The neurogenesis and cortical development**

My lab is interested in the function and regulation of neural stem cells in mammalian brains. We are working on 1) symmetric and asymmetric division of neuronal stem cells; 2) niches and neural differentiation of embryonic stem cells; 3) modelling human brain developmental diseases with pluripotent stem cells (PSCs); and 4) molecular and cellular mechanisms regulating neuronal stem cell fate and the development of the cerebral cortex.

**DR HUI YANG**

**Principal Investigator**  
**Institute of Neuroscience**  
**Chinese Academy of Sciences**  
**Email: huiyang@ion.ac.cn**



Hui Yang is Principal Investigator of the Institute of Neuroscience, Chinese Academy of Sciences. He is focusing on the mechanisms of early embryo development and reprogramming. In particular, he has made groundbreaking discoveries in the field of generation of genetically modified mice. He has

published 13 research articles in the most prestigious international journals including *Nature* and *Cell*. The establishment of two simple and highly efficient methods for generation of genetically modified mice has greatly facilitated the understanding and cure of human disease. Researchers are now studying ways to optimise methods for generating genetically modified non-human primates for modelling human disease.

**Poster title: Functional genomic screen in mice by CRISPR/Cas9-mediated genome engineering**

Genetically modified (GM) animals represent a crucial tool for understanding gene function in development and disease. Currently, GM animals can be generated by directly injecting DNA or mRNA of site-specific nucleases (ZNFs, TALENs, CRISPR/Cas system) into the one-cell embryo to generate DNA double-strand break (DSB) at a specified locus, which could drive both NHEJ-based gene disruption and homology directed repair (HDR)-based precise gene editing. However, the generation of GM animals by the CRISPR/Cas 9 system results in mosaicism, in which two or more populations of cells with different genomes are present in an individual animal. The limitation of this method

is longer gestational and sexual maturity lengths for phenotype analysis. Here, we developed a platform to the one-step generation of fully functional knockout mice by an optimised CRISPR/Cas9 system. With the optimised CRISPR/Cas9 system, the GFP gene or tyrosinase (Tyr) gene could be fully disrupted at first generation. Furthermore, we did a functional genomic screen on over 20 genes in mice and all of them could be well disrupted in one generation. These results provide a highly efficient method for functional genomic screening in mice.

**DR WEN ZHOU**

**Investigator**  
**Institute of Psychology**  
**Chinese Academy of Sciences**  
**Email: zhouw@psych.ac.cn**



Dr Wen Zhou (BSc, 2004 at Peking University; PhD, 2009 at Rice University) is an investigator at the Institute of Psychology, Chinese Academy of Sciences. She studies human olfaction, with particular interests in 1) the properties of human olfactory perception; 2) the extent to which human chemosignals are processed and recognised; and 3) the interplays between olfaction and other sensory (e.g. vision) and emotional systems.

**Poster title: Oxytocin mediates human chemosensory communication of gender in a dose-dependent manner**

We previously reported that two human steroids, androsta-4, 16,-dien-3-one and estra-1,3,5(10),16-tetraen-3-ol, respectively convey masculine and feminine information in manners contingent upon the recipient's gender and sexual orientation (*Current Biology*, 2014). Considering that sexual interactions are governed by internal physiological states, we have examined if oxytocin, a well-documented social neuropeptide that regulates sexual reproduction, mediates the decoding of chemosensory sexual cues. We show that nasally administered 24 IU of oxytocin disrupts the chemosensory decoding of feminine information in heterosexual males and that of masculine information in homosexual males, effects not found with vasopressin at the same dosage. At 12 IU, however, oxytocin, but not vasopressin, promotes the chemosensory decoding of feminine information in heterosexual males with autistic-like traits. Atosiban, a competitive antagonist of both oxytocin and vasopressin, abolishes the effect of chemosensory gender cues in both heterosexual and homosexual males. These results collectively demonstrate that oxytocin modulates human chemosensory communication of sexual information in a dose-dependent manner. Moreover, they provide fresh insights into the complex roles of oxytocin in social interplays.



