RHISE HBI-Melbourne Trainee Exchange

List of Supporting Laboratories for
2016

The following laboratories have expressed interest in participating in the exchange program. If potential applicants have other research interests, they should explore the University and Florey websites and make contact with relevant laboratory heads to determine whether they would be receptive to hosting a trainee under the auspices of this program.

UNIVERSITY OF MELBOURNE

1. **Neuroimmunology of Multiple Sclerosis** - Professor Trevor Kilpatrick

   Trevor Kilpatrick is a Professor of Neurology and Director of the Melbourne Neuroscience Institute at the University of Melbourne; he is the leader of the MS Division at the Florey Neuroscience Institutes and is a neurologist and Head of the MS Unit at the Royal Melbourne Hospital. His research interests include the neurobiology of multiple sclerosis, neural precursor cell biology and the study of genetic and environmental factors that contribute to MS as well as the translation of basic research discoveries to the clinic.

   **Current Projects:**
   I. The role of TAM receptor signalling in Central Nervous System Demyelination
   II. Functional consequences of Multiple Sclerosis risk genes
   III. Predicting, monitoring and altering outcome in MS

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2. **Neural Development, Injury and Pain Laboratory** - Professor Janet Keast/Dr Peregrine Osborne

   Our research is focused on the spinal cord and peripheral nervous system, especially in the contexts of autonomic function and visceral pain. Our primary goals are to understand the neurobiological causes of clinical conditions such as visceral pain and problems that arise from developmental disorders or disease of the urogenital system. This includes developing an understanding of the functional connectome of the lumbosacral autonomic system, in order to develop new ‘electroceutical’ therapeutic approaches.

   To address these questions, we use a variety of experimental approaches, including advanced microscopy, neuroanatomy, microsurgery, tract tracing, immunohistochemistry, image analysis, neuronal cultures, live cell imaging and behavioural testing.

   Some of our current research themes include:
   - Development and repair of spinal and peripheral autonomic nerve circuits
   - Mapping the functional connectome of sacral sensory and autonomic circuits
   - Mechanisms of establishing sexual dimorphism in the nervous system, and its implications for visceral pain and autonomic dysfunction
   - Visceral pain, especially investigating the plasticity of sensory neurons and spinal cord neurons that underlies development of chronic pelvic pain conditions (e.g., interstitial cystitis and endometriosis).
3. **Neurotrophin and Myelin Laboratory** - Dr Simon Murray/Dr Junhua Xiao

The research focus of the Neurotrophin Signalling Laboratory centres on a family of growth factors essential for normal nervous system function known as the neurotrophins. The laboratory is interested in the structure, biochemistry, and mechanisms of neurotrophin signalling, as well as several aspects of their biology, in particular the role they play in the myelinating process. In this regard, we are particularly interested in the impact that Brain Derived Neurotrophic Factor (BDNF) has upon the interactions between neurons and glial cells that regulate development of both central and peripheral myelin.

The myelin laboratory is interested in:
- Understanding the molecular and cellular bases that tightly control the differentiation, maturation and myelination of Schwann cells and oligodendroglia during development
- Understanding how myelin in maintained in adult life and during ageing
- Identifying factors that regulate myelin repair in acute and chronic models of demyelination
- Developing novel neurotrophin-based strategies in promoting myelin repair

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4. **Melbourne Brain Centre Imaging Unit** - Professor Roger Ordidge

The Melbourne Brain Centre Imaging Unit houses two state-of-the-art scanning facilities:
- Combined Positron Emission Tomography/ Computerised X-ray Tomography (PET/CT)
- 7-Tesla ultra high-field magnetic resonance imaging (MRI).

Current research projects include a number of studies on amyloid imaging, Alzheimer’s Disease, depression and traumatic brain injury. Professor Ordidge’s research interests include:
- Improvement of coverage of MRI methods at 7T, including development of 3D sequences for iron measurement that overcomes large scale susceptibility effects to obtain T2’, an improved 90 degree RF excitation pulse that is tolerant of B1 non-uniformity and application of above RF pulse with adiabatic 180 degree pulses.
- 7T Sodium Imaging: Head Imaging in Traumatic Brain Injury and MS.
- PET/CT: Investigation of hypo-intensity tracer signals in damaged white matter.

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5. **Human Pluripotent Stem Cell Laboratory** - Professor Martin Pera

Professor Pera’s laboratory is focused on the extrinsic mechanisms that regulate self-renewal and early lineage commitment of human pluripotent stem cells. The group is particularly interested in early neural progenitors and the development of human cortical neurons. We are also studying a new marker for progenitor populations in tissues of endodermal origin, which has applications in isolation and characterization of normal and malignant liver and pancreatic progenitor cells.

The Stem Cells Australia initiative has been established by the University of Melbourne, Monash University, University of Queensland, University of New South Wales, Walter and Eliza Hall Institute for Medical Research (WEHI), Victor Chang Cardiac Research Institute, Florey Neuroscience Institutes and CSIRO.
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6. **Imaging cellular structure and function in the living retina** - Assoc. Professor Andrew Metha
Our broad research aim is to understand the fundamental workings of the living retina on the microscopic scale, and how this becomes compromised in sight-debilitating diseases such as diabetes and glaucoma. We combine a range of investigative tools including high-resolution non-invasive imaging, psychophysics, computational modelling and electrophysiology.

Our current research projects make use of high speed, multi-spectral adaptive optics to visualize the smallest neurons, glial cells and blood vessels in living eyes of humans and animals. We study the dynamics of flow and oxygen exchange at the level of individual red blood cells. We study the cascade of optical and physiological events that occur when a photoreceptor interacts with light. In our dedicated animal imaging laboratory at the new Melbourne Brain Centre facility, we also use microscopic cellular labelling techniques to study the earliest stages of retinal disease.

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7. **Central Cardiovascular Regulation** - Professor Andrew Allen
Andrew’s research group has an overarching interest in how the central nervous system modulates cardiovascular function via the autonomic nervous system. This encompasses an interest in neuroscience, particularly how neural groups interact in vivo to generate specific motor patterns (in this case sympathetic activity to vascular smooth muscle), as well as the cardiovascular system.

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8. **The Melbourne Neuropsychiatry Centre**
The Melbourne Neuropsychiatry Centre (MNC) is a joint centre of Melbourne Health (North West Mental Health) and The University of Melbourne (Department of Psychiatry). It comprises the Neuropsychiatry Unit at Royal Melbourne Hospital (RMH), the Cognitive Neuropsychiatry Unit and Adult Mental Health Rehabilitation Unit at Sunshine Hospital, and the Neuropsychiatry Imaging Laboratory located at the National Neuroscience Facility within The University of Melbourne, Parkville. The goals of the MNC are:

- To improve our understanding of disorders of the brain and mind
- To improve the quality of care for patients with complex mental health problems and disorders
- To establish a Victorian neuropsychiatry centre of clinical, research and academic excellence, which ensures that specialised knowledge and skill become part of everyday clinical practice
- To provide neuropsychiatric training and education to mental health professionals and other health disciplines

Contact Details:
PSYCHOSIS AND DEVELOPMENTAL NEUROPSYCHIATRY
Prof Christos Pantelis & Dr Vanessa Cropley
Neurobiological basis of disorders. Pattern and timing of changes.
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CLINICAL NEUROPSYCHIATRY
Prof Dennis Velakoulis
Neuropsychiatric assessment and advice.
9. **The Epilepsy, TBI and Neuropharmacology Research Groups** – Prof. Terry O’Brien

*Department of Medicine, The Royal Melbourne Hospital.*

The research of our Group is broad-based, covering both basic and clinical studies into epilepsy and related areas, including traumatic brain injury and dementing disorders. The Group’s Research has two primary goals: First, to better understand the determinants of treatment response by identifying biomarkers for treatment outcomes – imaging, electrophysiological, genomic and clinical, and to develop new treatment approaches. Second, to investigate the fundamental neurobiological basis of the neuropsychiatric co-morbidities present in many patients with epilepsy and related conditions.

Specific project areas include:

- Application of novel imaging approaches to clinical and basic studies.
- The effects of exposure to anti-epileptic drugs on the developing foetus.
- The neurobiological link between epilepsy, brain injury and psychiatric co-morbidities.
- Pre-clinical development of novel therapies for epilepsy and neurodegenerative diseases (this includes being one the PI sites for the NINDS funded EpiBios4Rx Centre without Walls Grant into developing anti-epileptogenic therapies).
- Translation of basic research to early stage clinical trials.
- Cohort studies of outcome of epilepsy and its treatments, and identification of clinical, EEG and imaging biomarkers.

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10. **Epilepsy and behaviour laboratory – Assoc. Prof. Nigel Jones**

Our research utilises basic science approaches to explore animal behaviour in the context of health and disease. The primary goal of the lab is to understand the pathophysiological mechanisms which cause neurological and neuropsychiatric disorders, particularly epilepsy, cognitive disorders and mental health conditions. We employ a range of advanced behavioural tests of cognition, anxiety, depression, coupled with in vivo electrophysiology, molecular biology, in vivo imaging, opto/chemogenetic, immunocytochemical and transgenic methods to achieve this goal. We also study the role and influence of neuronal oscillations in cognitive behaviours in physiological circumstances, using sophisticated behavioural tasks and high-end electrophysiological recordings.

**Current available projects:**
- Effects of stress on epilepsy and seizures
- Effects of antidepressants in epilepsy
- Consequences of epilepsy on affective and cognitive behaviours
- Effects of hallucinogenic drugs on cognition and electrophysiology

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FLOREY INSTITUTE OF NEUROSCIENCE AND MENTAL HEALTH

1. **STROKE DIVISION** – Professor Julie Bernhardt & Prof. Vincent Thijs (Co-heads of Stroke Division)

The Florey stroke division is a vibrant interdisciplinary group dedicated to the study of stroke from a basic science level through to public health, rehabilitation and epidemiology. The division is host to Australia’s first NHMRC Centre for Research Excellence in Stroke Rehabilitation and Brain Recovery. We investigate neuroprotective and neuroregenerative drugs, brain biology and response to interventions with advanced imaging, new approaches to improving stroke health service delivery, including telehealth, and we help build the evidence base for stroke care using world class clinical trials methods.

Current projects within the public health and health services group that may be of interest include:

*Victorian Stroke Telemedicine program*: international minimum dataset project and comparison of acute stroke telemedicine programs around the world

*Australian Stroke Clinical Registry*:
  a) Building the potential for comparative analyses with Canada and Australia on the quality of care for patients experiencing acute stroke and outcomes.
  b) Project on young stroke (age under 55 years) in collaboration with The George Institute of Global Health
  c) Examples of current projects in the AVERT early intervention and exercise group include:
     a. Who recovers and who doesn’t? – exploring the large AVERT trial dataset (n>2000) to identify clinical phenotypes to better stratify clinical trials
     b. Improving outcomes in clinical stroke recovery trials – getting to a minimum dataset
     c. Young stroke recovery – examining return to work and resource use in those under 55

Check out the Florey website for more details

Prof. Vincent Thijs is the Head of Stroke at Austin Health (since 2015).

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2. **BEHAVIOURAL NEUROSCIENCE DIVISION** – Co-Heads Prof. Andrew Lawrence & Dr Amy Brodtmann

Our Addiction group investigates how alcohol and drugs can change the brain’s structure, chemistry and function. Genetic approaches combined with animal models of drug-seeking and relapse can help examine neural pathways implicated in drug seeking behaviour.

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**Clinical Cognitive Neuroscience Laboratory** - Dr. Amy Brodtman

In the Clinical Cognitive Neuroscience Laboratory, we study network degeneration following brain injury (e.g., ischaemic stroke) and have a particular interest in vascular contributions to cognitive impairment both in aging and in a range of neurodegenerative diseases, such as Alzheimer’s disease (AD). The latter is the most common cause of dementia in the western world and is associated with profound impairments in cognition and activities of daily living. Our research seeks to investigate neuroimaging correlates of cognitive decline; the effects of post-stroke exercise interventions on brain volume and cognitive function; and the accuracy and accessibility of imaging modalities in the diagnosis of dementia. The ultimate goal of
our research is to increase our understanding of two of the major causes of death, disability, and reduced quality of life in our society: dementia and stroke.

**Vascular Neurodegeneration Research Laboratory - Dr. Amy Brodtman**

Stroke and dementia are linked. Up to two thirds of people who have a stroke experience cognitive impairment, and more than one third will develop dementia over the subsequent five years. Moreover, risk factors for stroke and dementia are similar. Yet we still know very little about whether brain volume loss – a hallmark of dementia – occurs after stroke, and whether such atrophy is related to cognitive decline. An understanding of whether stroke is neurodegenerative, and in which patients, may be used to help guide the early delivery of disease-modifying therapies.

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**Epigenetics and Neural Plasticity Laboratory - Professor Anthony Hannan**

The Epigenetics and Neural Plasticity Laboratory investigates gene-environment interactions and experience-dependent plasticity in the healthy and diseased brain, using a variety of experimental approaches. This includes research using a model of Huntington’s disease (HD), a tandem repeat disorder, where we are following up our discoveries regarding the beneficial effects of environmental enrichment (enhanced cognitive stimulation and physical activity) and exercise, as well as depression and dementia-like symptoms associated with abnormalities of brain plasticity. Furthermore, we recently discovered that chronic stress can accelerate onset of HD, and are investigating these neurotoxic effects of stress in HD and other brain disorders.

Many neurological and psychiatric disorders have their origins in abnormal maturation of the brain, including the billions of neurons exquisitely connected by trillions of synapses.

We are also investigating how genetic and environmental factors combine to cause specific disorders of brain development and cognition, including schizophrenia and autism spectrum disorders (ASD). We are interested in the mechanisms whereby specific genes regulate maturation of the brain and are dynamically regulated by interaction with the environment in conditions like ASD and schizophrenia.

Our research links data at behavioural and cognitive levels to underlying cellular and molecular mechanisms. We use a variety of behavioural tools, including automated touchscreen testing of cognition and high-throughput data analysis of vocalization and communication that are directly translatable to clinical tests. We are establishing the extent to which experience-dependent plasticity, including adult neurogenesis and synaptic plasticity, can modulate these behavioural and cognitive endophenotypes, in models with targeted genome editing. This cellular level of understanding is linked, in turn, to molecular mechanisms, including epigenetics, transcriptomics and proteomics.

Based on this research, and the identification of key target molecules, we are also exploring the concept of ‘enviroimimetics’, therapeutics that mimic or enhance the beneficial effects of cognitive stimulation and physical exercise. One goal is to develop such therapeutic agents to help reduce the personal and societal burdens of devastating brain disorders such as schizophrenia, HD and dementia.

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3. **Brain Development and Regeneration** – Prof. Seong Seng Tan

The Brain Development group dedicates its research focus to discovering how newly born neurons are properly assembled, interconnected and electrically activated. In particular, the group is interested in how immature brain cells in the embryonic brain know where to go, what to become, what other cells they should be connect to.

The Traumatic Brain and Stroke group is actively engaged in exploiting pre-existing protective mechanisms to prevent neurons from dying after injury. They are interested in identifying drugs that will up-regulate concentrations of Ndfip1, a naturally occurring protein that is present in low concentrations in brain cells, but is massively increased in surviving neurons after brain injury.

The group has made significant progress in understanding how Ndfip1 improves the survival of brain cells after injury. In animal models, it has demonstrated that Ddfip1 is increased in surviving neurons after experimentally induced stroke.

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4. **Epilepsy** – Prof. Graeme Jackson and Assoc. Prof. Steve Petrou

Epilepsy is a debilitating brain disease that afflicts 10 percent of the population at some stage. Our laboratory has taken the approach that novel opportunities for therapeutic intervention will arise by; 1) the creation of syndrome-specific epilepsy models based on human genetic lesions and; 2) a detailed analysis of the fundamental mechanisms that underlie disease genesis and progression in these models.

We employ a multidisciplinary approach that combines molecular biology, biophysics, computer modelling, single cell and brain slice electrophysiology, macro and micro histological digital imaging, EEG, unit recording and in vivo patch clamp in brains and behavioural analysis of mice. By studying the effects of epilepsy gene mutations at several levels of functional organisation, we can validate our models against the human conditions and then delve into the mechanisms of seizure genesis.

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5. **NEURODEGENERATION DIVISION** – Co-Heads Prof. Colin Masters and Prof. Phil Beart

The Neurodegeneration Division comprises around 20 different laboratories. More information on laboratories and projects can be found at the following link: https://www.florey.edu.au/neurodegeneration-division

Some key laboratories and their research focus are outlined below, however interested potential exchange scholars are encouraged to check the website and Division Heads for further detail.

**Oxidative Biology Unit - Professor Ashley Bush**

Professor Ashley Bush and his group are looking at how key proteins interact inappropriately with metals in the brain to cause “oxidative stress” in diseases including Alzheimer’s and Parkinson’s disease. They are actively working to develop a disease-modifying drug for Alzheimer’s disease, with one currently in clinical trials.

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Neuropathology and Neurodegeneration Laboratory – Prof. Colin Masters
Understanding the molecular basis of Alzheimer’s disease is the main focus of this laboratory. We aim to identify the specific conformer of the Aβ amyloid peptide which accumulates in Alzheimer’s disease brain. In both familial early onset Alzheimer’s disease (in which Aβ is over-produced) and in late onset sporadic Alzheimer’s disease (in which Aβ is poorly cleared from the brain), the same underlying process causes the synapses in the brain to degenerate. Based on this knowledge, we are able to seek biomarkers in the CSF and blood and to discover suitable lead compounds which can target the Aβ oligomer itself.

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6. DIVISION OF BIOLOGICAL PSYCHIATRY & MENTAL HEALTH
Molecular Psychiatry Laboratory - Prof. Brain Dean
Professor Brian Dean and his team are looking at post-mortem brain tissue in an attempt to see what is different in the brains of people who had a mental illness. They believe that schizophrenia is a syndrome made up of a number of diseases. By identifying and describing these, researchers hope to enable more targeted and effective treatments.

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7. Neuropeptides – Prof. Ross Bathgate
Neuropeptides act by binding to and activating receptors that are located on the surface of their target cells. In humans, the major class of neuropeptide receptors are from the G protein-coupled receptor (GPCR) family, the largest gene family in the human genome. GPCRs are involved in controlling virtually every physiological process in our bodies and thus are the major class of proteins through which prescription drugs illicit their actions. The Neuropeptides Division studies numerous peptide systems which target GPCRs. The focus is on determining how the peptides function in normal biology to determine how they can best be used to treat human diseases. These studies are coupled with fundamental drug discovery, with the aim of developing drugs that mimic these native peptides to treat vascular, fibrotic, metabolic and psychiatric diseases.

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8. Peptide Neurobiology Laboratory – Prof. Andrew Gundlach
Professor Andrew Gundlach and his team in the Peptide Neurobiology Laboratory investigate key aspects of the neurobiology of relaxin-3 signalling in mammalian brain circuits, including details of their anatomical connectivity, neurochemistry, physiology and impact on behaviour, under normal conditions and in neurodegenerative and psychiatric diseases. Genetic, viral and pharmacological approaches combined with studies of normal and transgenic animals aim to identify neural pathways involved in arousal, stress-related, motivated and affective behaviours and related cognitive processes, with a focus on the 'nucleus incertus' and the therapeutic potential of targeting relaxin-3 receptors.

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9. **Systems Neurophysiology – Prof. Robin McAllen**

The focus of this division is on how the brain and peripheral nervous system control vital body functions in health and disease.

Profs. Robin McAllen, Prof Michael McKinley and colleagues study how the brain communicates with the immune system to regulate inflammation. They also study how the brain regulates body temperature, fluid balance and the cardiovascular system.

Prof. Clive May and colleagues are studying how clinical improvements may be made in a range of medical conditions including heart failure and sepsis, focusing on the role of the nervous system.

A/Prof. Mathias Dutschmann and colleagues investigate the brainstem circuitry that regulates respiration and the control of the airways. A particular focus is on the neuroplasticity of these control circuits and their vulnerability in neurodegenerative disease.

Dr. Song Yao studies the role of new born neurons in the brain stem circuits regulating cardiovascular and other homeostatic functions. A second project investigates the role of the blood brain barrier, particularly in the hypothalamus, in hypertension and heart failure.

Dr Stuart McDougall investigates synaptic mechanisms in the brain stem, with a focus on how visceral afferent signaling is integrated with central processes for the control of homeostatic functions.

Prof. John Furness manages a range of investigations that focus on the gastrointestinal tract and its neural and hormonal control.

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10. **Neural Networks Laboratory - Dr. Lucy Palmer**

The Palmer Laboratory aims to understand the neural activity contributing to perception and behaviour in the mammalian brain. Individual neurons are continuously bombarded with thousands of synaptic inputs which must integrate to generate an internal representation of the external environment. We investigate how the brain processes this sensory information by measuring the activity of neurons within the neocortex in vivo using a variety of techniques including two photon calcium imaging, somatic and dendritic patch-clamp recordings and optogenetics.

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