THE UNIVERSITY OF MELBOURNE

ANATOMY AND NEUROSCIENCE 2021

RESEARCH PROJECTS HONOURS, MASTERS AND PHD

WELCOME

The department of Anatomy and Neuroscience provides a wide range of opportunities for students to undertake biomedical research.

Most of these projects fall within our largest research concentrations, Cell and Developmental Biology, and Neuroscience, but you will also see projects from our emerging research specialisations (such as Human Anatomical Research), and many Neuroscience projects offered by our colleagues from the Florey Institute for Neuroscience and Mental Health.

These projects are typically available as the research component for course-work degrees (Honours, and the Master of Biomedical Science), or as a much more extended research project for the M.Phil. or Ph.D. research degrees.

In all cases, your enrolment has two components: eligibility (the eligibility criteria are described in this booklet and on the relevant websites) and selection. Selection means selecting projects you most like and obtaining agreement from the supervisor of that project that it will be available to you. The purpose of this booklet is to help with the process of selection by showcasing our research projects and providing the contact details of potential supervisors*.

The department also holds a research project information session. This is a great opportunity to speak with potential supervisors (and current research students) about the projects on offer. Our information session will be held on Friday 18th September 2020, in the Harry Brookes Allen Museum of Anatomy and Pathology Museum - see our website for details).

No matter what project you might choose, you will be pursuing an important and challenging question in biomedicine, and you will be supported by state-of-the-art facilities and a lively and congenial community of researchers.

I look forward to meeting you in the Department

J. Wilkinson-Berka

Professor Jennifer Wilkinson-Berka

Head, Department of Anatomy and Neuroscience
School of Biomedical Science,
The University of Melbourne

HOW TO APPLY

HONOURS

What is Honours?

Honours is a fourth-year undergraduate course that consists of a combination of a research project and coursework subjects. The course is designed to develop the student's capacity to solve problems, to analyse data, to read and think critically, and to communicate clearly.

Honours can give you a taste of what working as a scientist would be like as a career, allows you to demonstrate academic excellence in an area of special interest to you, and provides an entry point for further research higher degree study (i.e. PhD). These skills are highly sought after by employers in biological, medical and industrial areas.

What are the entry requirements?

To be considered for entry, applicants must have completed a suitable undergraduate degree (Bachelor of Biomedicine, Bachelor of Science or equivalent) with a major in a relevant discipline with a WAM (weighted average mark) of at least H3 (65%) or equivalent.

Students who have completed or are due to complete a Bachelor of Biomedicine at the University of Melbourne should apply to complete Biomedicine Honours. Students who have completed or are due to complete a Bachelor of Science at the University of Melbourne or an equivalent course at another institution should apply to complete Science Honours.

Meeting the minimum Faculty level is not a guarantee of admission and students must be accepted by a supervisor before entry into the course.

How long is Honours?

Honours is a one-year course consisting of 75 points of research and 25 points of coursework, that commences mid-February and finishes in November.

How to apply

STEP 1: Contact Potential Supervisor(s)

Decide which departments, institutes, supervisors and projects you wish to apply for and make contact with the relevant supervisor.

Applicants must contact potential supervisors either before or soon after submitting an online application for entry to an MDHS Honours course. Department and Institute Honours project booklets and websites, the individual information sessions held by departments and institutes are ways of helping you to make initial contact with potential Honours supervisors. However, if you are seriously considering a project you should arrange to meet your potential supervisor more formally to get a much better idea about the project and their expectations.

STEP 2: Online Application

Lodge an online application

1. Apply online and select either the Returning Applicants, Current Students and Previous Students or First Time Applicants. Do not select the First Time Applicants option if you have previously completed study or applied to any program at The University of Melbourne.
2. Select 'MDHS Specialisations' as requirement response in the online application form.
3. Provide original or certified transcript(s) for any study not undertaken at The University of Melbourne. You are not required to provide transcripts for study undertaken at this university.

STEP 3: Project Preference

Once you have submitted an online course application, you will receive an email within 3 working days with your personal login details to access the Honours Project Preference System - SONIA. Please follow the instruction in the email to set up your password and select your preferences for projects offered within MDHS departments. You may select up to 4 project preferences in Round 1 or 3 project preferences in Round 2 and 3. You must only preference projects after making contact with the relevant supervisor(s). You are allowed to log into Sonia to change your preferences any time by the closing date.

More information including application dates and online application link: mdhs-study.unimelb.edu.au/degrees/honours/apply-now

MASTER OF BIOMEDICAL SCIENCE

What is the Master of Biomedical Science?

The Master of Biomedical Science at the University of Melbourne is a coursework master's degree incorporating a substantial research project. This course is an alternative to the Honours as a PhD pathway. Students undertake a major research project and discipline-specific coursework subjects. In addition, a suite of professional business and communication subjects are offered to complement and enhance the research undertaken and to progress students' career opportunities.

The course encourages students to think innovatively and provides an awareness of the health and economic benefits of biomedical research. Graduates of this course gain an understanding of the research process, specialist knowledge and professional skills that are attractive to employers.

What are the entry requirements?

To be considered for entry, applicants must have completed a suitable undergraduate degree with a major in a relevant discipline with a WAM (weighted average mark) of at least H3 (65%) or equivalent. Meeting this requirement does not guarantee selection.

Note

- Quotas may be applied to the degree as a whole, or to individual disciplines, and preference may be given to applicants with evidence of appropriate preparation or potential to undertake research.
- Entry is subject to the capacity of a participating department to provide adequate supervision in a research project appropriate to the interests and preparation of the individual student and is subject to the agreement of an academic staff member to supervise the project.
- Students entering this course are expected to organise an academic supervisor in the relevant academic unit, and select a research project, as part of the application process. You will be provided with a list of current projects once your application has been assessed and deemed eligible. The theme and scope of the research project is negotiated between the student and supervisor prior to commencement of the course.

How long is the Masters of Biomedical Science?

The Masters is a two-year (full time) course consisting of 125 points of research and 75 points of coursework. The course can be commenced at the start of the year or at mid-year.

How to apply

1. Apply online and select either Current Students and Previous Students or First Time Applicants. Do not select the First Time Applicants option if you have previously completed study or applied to any program at The University of Melbourne.
2. Provide original or certified transcript(s) for any study not undertaken at The University of Melbourne.

Selecting a Project

Once you have submitted an online course application, you will receive an email with your personal login details to access the Master of Biomedical Science Project Preference System - SONIA. Please follow the instruction in the email to set up your password and review projects offered within MDHS departments. You must make direct contact with the supervisor and obtain permission to work on their project before submitting your project preference. Once your project has been endorsed, you will be allocated to this project in SONIA.

More information including application dates and online application link: study.unimelb.edu.au/find/courses/graduate/master-of-biomedical-science/how-to-apply/

Difference between Honours and the Master of Biomedical Science

	Honours	Masters
Duration	1 year (full time)	2 years (full time), part time available
Level	Undergraduate	Graduate
CSP (commonwealth supported places) available?	Yes	Limited
PhD Scholarship scoring	Considers marks from 3rd year of Bachelor's degree and Honours marks	Only Masters marks are considered
International Market recognition	Australian Honours degrees may not be recognised overseas, as many countries do not have an equivalent degree.	Recognised as a graduate master's degree

RESEARCH HIGHER DEGREES

What is a PhD?

A PhD (Doctor of Philosophy) is a 3-year supervised research degree with the possibility of up to 12 months extension. A candidate may be required to supplement their research with enrolment in additional subjects if considered necessary. The research is written up as a thesis (80,000 – 100,000 words) and examined by external experts in the field.

What is a MPhil?

A MPhil (Master of Philosophy) is similar to a PhD but carried out over a shorter period of time of 18months to 2 years. The research work is written up as a thesis (30,000 – 40,000 words) which demonstrates your knowledge and contribution to the field of research.

What are the entry requirements?

To be considered for entry into a PhD, applicants must have completed

- a four-year Bachelor degree (BSc Hons, BBiomed Hons) in a relevant discipline which includes a substantial research component equivalent to at least 25% of one year full time study and achieved a minimum WAM of 80% (university of Melbourne) or equivalent; or
- a Masters degree in a relevant discipline which includes a substantial research component equivalent to at least 25% of one year of full time study and achieved a minimum weighted average of 80% or (University of Melbourne) equivalent.

To be considered for entry into a MPhil, applicants must have completed

- a four-year Bachelor degree (BSc Hons, BBiomed Hons) in a relevant discipline which includes a substantial research component equivalent to at least 25% of one year full time study and achieved a minimum WAM of 75% or higher; or
- a Masters degree in a relevant discipline which includes a substantial research component equivalent to at least 25% of one year of full-time study and achieved a minimum weighted average of (University of Melbourne) 75% or higher.

Choosing a supervisor and research area

A critical element of success is choosing a research area that interests you. Departmental websites have information on the range of research areas on offer, as well as areas of interest of academic staff members who can supervise your project.

It is very important for you to talk to supervisors as well as current or previous students. It is one thing to be interested in the project but you need to get along with your supervisor too. If possible, try to get some work experience in the lab to get an idea about the environment.

For future information regarding Research Higher Degrees at the University of Melbourne see the following links:

study.unimelb.edu.au/find/courses/graduate/doctor-of-philosophy-medicine-dentistry-and-health-sciences/

study.unimelb.edu.au/find/courses/graduate/master-of-philosophy-mdhs-biomedical-science/

How to apply

1. Review the list of prospective projects and supervisors in this handbook or online at biomedicalsciences.unimelb.edu.au/departments/pharmacology#research
2. Identify projects of interest and contact the project supervisor to explain your research interests and provide your curriculum vitae (CV) can academic transcripts.
3. Once confirmed a project and supervisor apply online at study.unimelb.edu.au/how-to-apply/graduate-research

SCHOLARSHIPS

Honours

Honours applicants who accept and enrol in an Honours course will automatically be considered for available Honours Scholarships. These are awarded on academic merit.

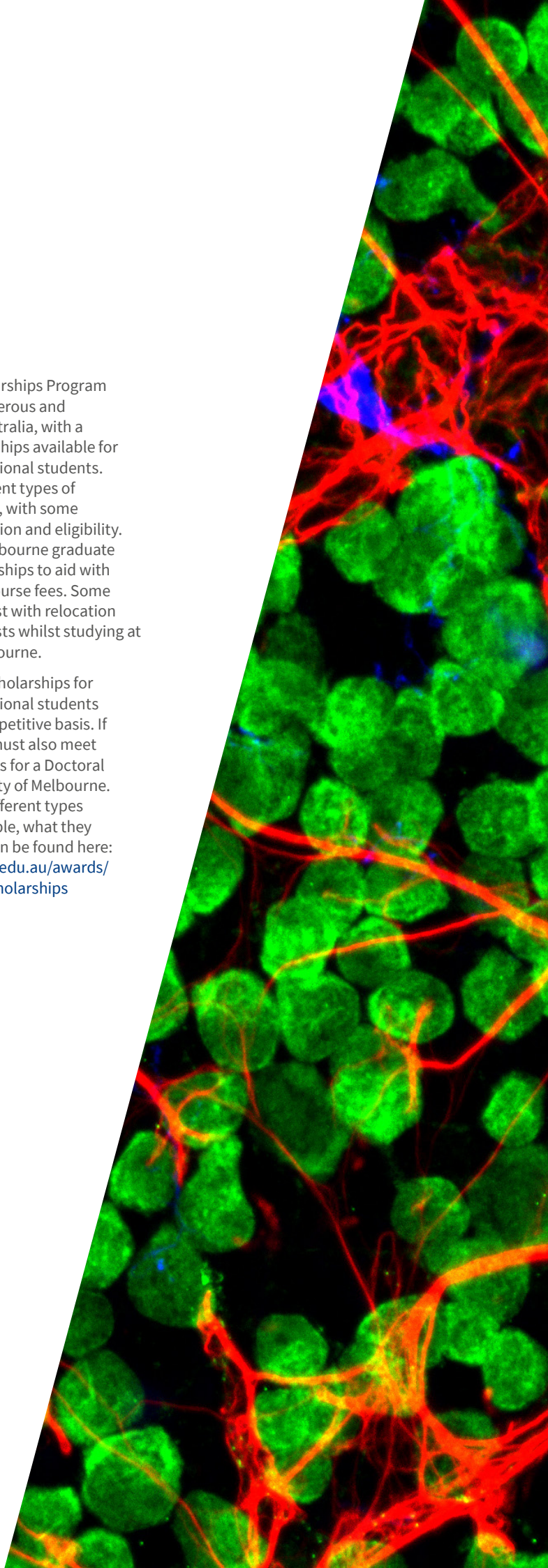
Highly ranked full-time students who have enrolled in an MDHS program through the Bachelor of Biomedicine (Degree with Honours) and the Bachelor of Science (Degree with Honours) and demonstrated a level of financial needs will automatically be considered for an Frances Elizabeth Thomson Trust Scholarship. The Scholarship will award eligible students with a one- off payment of $5,000. mdhs.unimelb.edu.au/study/ scholarships/n/frances-elizabeth-thomson

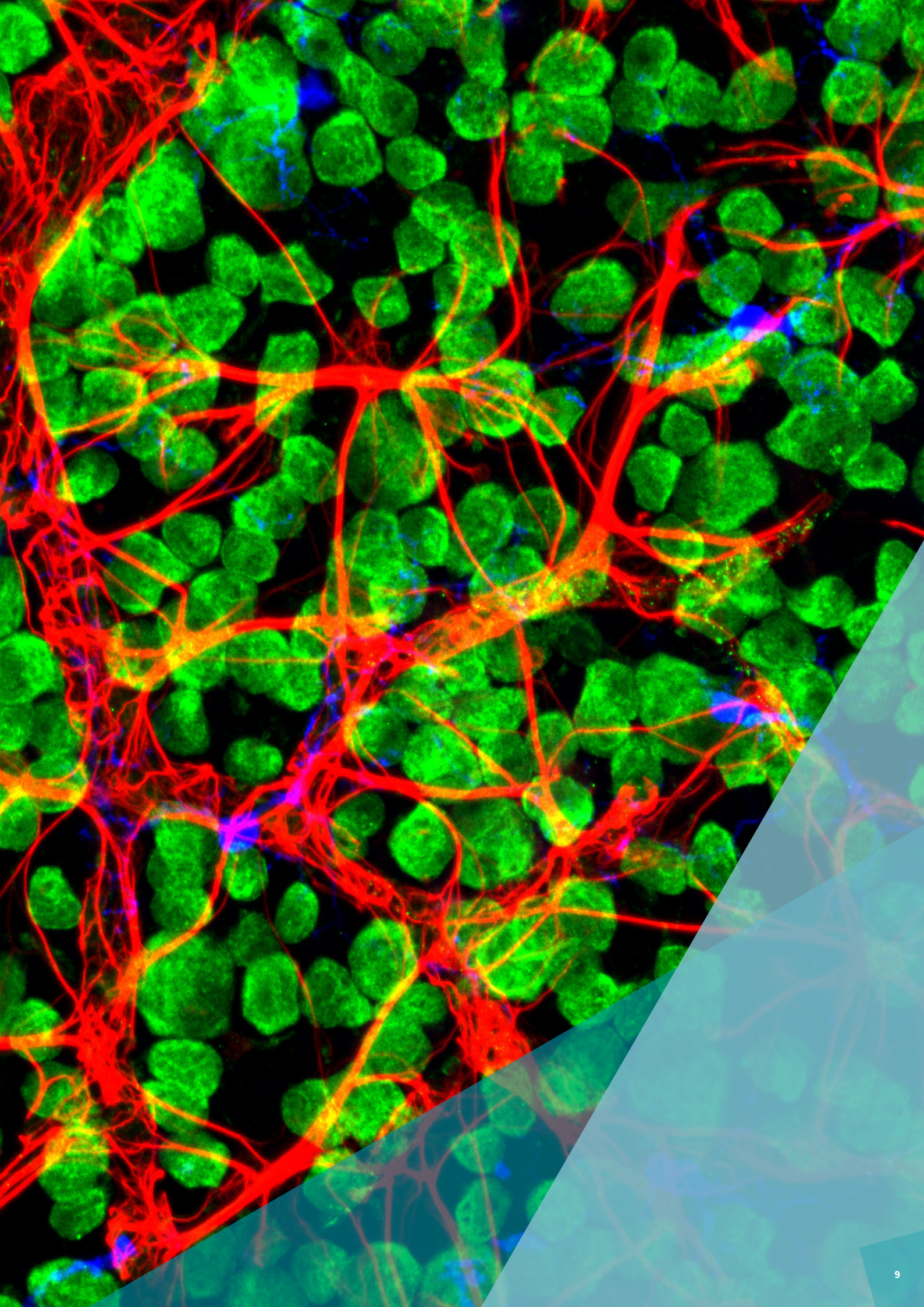
The Dept. of Pharmacology and Therapeutics offers financial support for Honours/Masters students to attend and present their research at a scientific conference commonly, The Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT).

Graduate degrees

The Melbourne Scholarships Program is one of the most generous and comprehensive in Australia, with a wide range of scholarships available for domestic and international students. There are many different types of scholarships available, with some varying in value, duration and eligibility. Most University of Melbourne graduate students have scholarships to aid with living expenses and course fees. Some scholarships also assist with relocation fees and insurance costs whilst studying at the University of Melbourne.

Graduate Research Scholarships for domestic and international students are awarded on a competitive basis. If successful, students must also meet the entry requirements for a Doctoral degree at the University of Melbourne. More details on the different types of scholarships available, what they cover and eligibility can be found here: scholarships.unimelb.edu.au/awards/graduate-research-scholarships





PROJECTS

ACKLAND GROUP

Contact: **Dr. David Ackland**
Email: **dackland@unimelb.edu.au**
Location: **Department of Biomedical Engineering, University of Melbourne**

A/Prof Ackland's Orthopaedic Biomechanics group investigates the human musculoskeletal system, and surgical procedures to restore function in conditions such as osteoarthritis, tumour resection, congenital abnormalities, and trauma. We have established expertise in experimental and computational approaches to examining the structure and function of bones and joints including those of the jaw, neck, hip, knee, shoulder and foot.

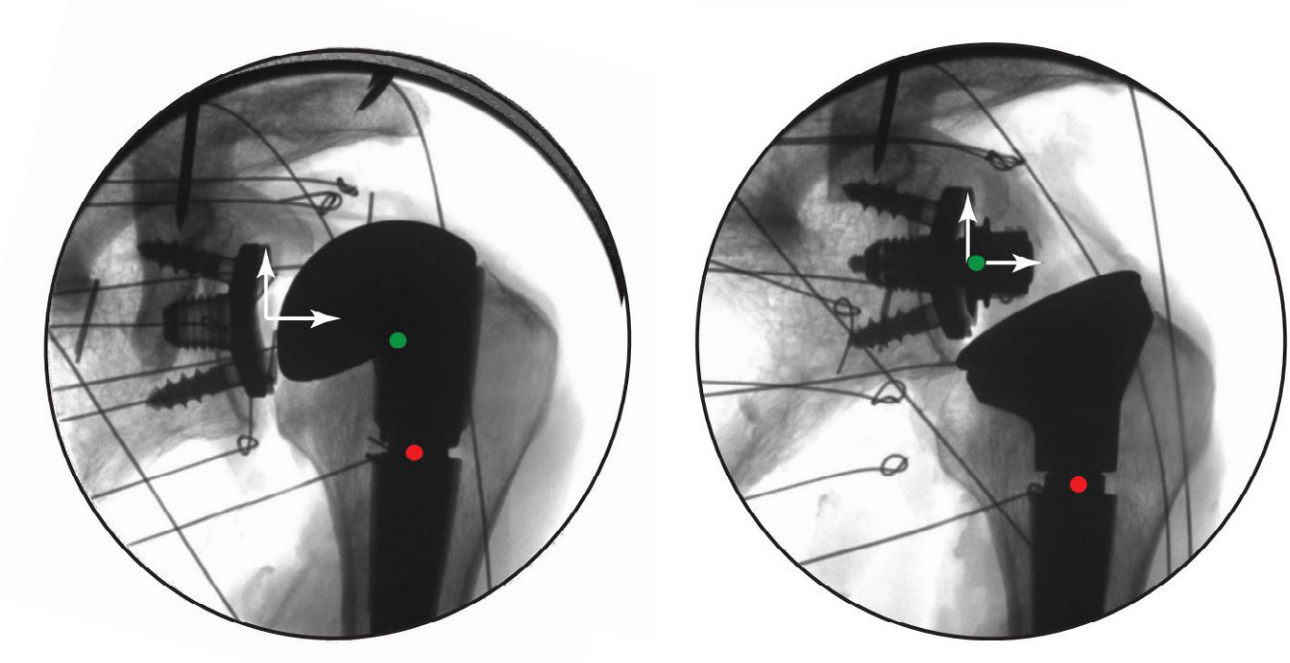
Project: Rotator cuff tears in the human shoulder

Rotator cuff tears remain one of the most common causes of joint instability and dysfunction in the human shoulder, yet the function of the rotator cuff tears in stabilising the shoulder are frequently debated. The aim of this project is to evaluate function of the shoulder in the presence of progressive rotator cuff tears, and to evaluate the capacity of surgical repair of torn tendon in restoring joint behaviour. The aim will be achieved using state-of-the-art cadaveric testing and motion experiments to examine joint motion, joint space volume and impingement of the humerus on the acromion – a mechanism thought to exacerbate rotator cuff tearing and joint dysfunction. The project outcomes will provide new information on the roles of the rotator cuff muscles and guide surgical technique in rotator cuff reconstruction. This Honours project will involve close collaboration with orthopaedic surgeons from Epworth Healthcare. Prior knowledge of engineering is not required; however, an understanding of musculoskeletal shoulder anatomy will be very useful.

Project supervisor
Dr David Ackland

Project co-supervisor
A/Prof Martin Richardson
(Epworth Healthcare)

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science



Shoulder after anatomical total shoulder arthroplasty (left) and reverse total shoulder arthroplasty (right)".

BARTON GROUP

Contact: **Dr. Samantha Barton**

Email: **samantha.barton@florey.edu.au**

Location: **Florey Institute of Neuroscience and Mental Health**

Dr Barton's laboratory focusses on the motor neurone diseases and frontotemperal dementia, especially the role of non-neuronal cells like oligodendrocytes.

Project: Using the SOD1G93A MND mouse model to determine the role of oligodendrocytes in disease

Oligodendrocytes have two essential roles in the CNS – to myelinate neurons and to provide metabolic support to axon through this myelin sheath. Given more than 95% of a neuron is its axon, and axons require myelination for normal function, impaired oligodendrocyte function would negatively impact on myelin formation and subsequent capacity to metabolically support neurons. Indeed, recent research from our lab and others has begun to implicate oligodendrocyte dysfunction in MND pathogenesis. This project will use a combination of biochemical approaches to assess gene and protein expression as well as advanced imaging techniques like SCoRe which isn't available anywhere else in Australia and allows an in depth analysis of myelination. This can be coupled with electron microscopy to give a very thorough evaluation of oligodendrocyte function in MND; this will be a critically important study in the field particularly given the current interest in glial involvement in MND.

Project supervisor
Dr Samantha Barton

Project co-supervisor
Dr David Gonsalvez
Dr Bradley Turner

- M.Phil/Ph.D.
- Honours

Project: Using the TDP-43Q331K MND mouse model to determine the role of oligodendrocytes in disease

Oligodendrocytes have two essential roles in the CNS – to myelinate neurons and to provide metabolic support to axon through this myelin sheath. Given more than 95% of a neuron is its axon, and axons require myelination for normal function, impaired oligodendrocyte function would negatively impact on myelin formation and subsequent capacity to metabolically support neurons. Indeed, recent research from our lab and others has begun to implicate oligodendrocyte dysfunction in MND pathogenesis. This project will use a combination of biochemical approaches to assess gene and protein expression as well as advanced imaging techniques like SCoRe which isn't available anywhere else in Australia and allows an in-depth analysis of myelination. This can be coupled with electron microscopy to give a very thorough evaluation of oligodendrocyte function in MND; this will be a critically important study in the field particularly given the current interest in glial involvement in MND.

Project supervisor
Dr Samantha Barton

Project co-supervisor
Dr David Gonsalvez
Dr Bradley Turner

- M.Phil/Ph.D.
- Honours

BOOTH GROUP

Contact: **Dr. Lindsea Booth**

Email: **lindsea.booth@florey.edu.au**

Location: **Florey Institute of Neuroscience and Mental Health**

The cardiovascular branch of the Preclinical Critical Care Group at the Florey Institute is focused on understanding how genetic, neurochemical and structural changes that occur in the brain in cardiovascular disease, for example heart failure, contribute to changes in the autonomic nervous system and consequently disease progression.

Project: Using optogenetics to stimulate the vagus in heart failure

Heart failure is an epidemic of the third millennium, affecting an increasing number of Australians. Heart failure patients have a 5-year mortality rate of 75% and cost the health care system ~A$2.7 billion/year. Improved treatments to slow the progression and hospitalisation due to heart failure are required. High cardiac sympathetic drive and impaired vagal tone are powerful predictors of fatal arrhythmias and worsening cardiac function in heart failure. We have strong preliminary data showing that selective stimulation of a distinct subset of vagal fibres, rather than stimulation of the whole nerve, improves cardiac function in heart failure.

The current project uses optogenetic techniques to selectively activate efferent projections of the vagus nerve in a large animal model of heart failure. Investigate the changes in cardiac function (measuring contractility, ejection fraction, blood hormone levels) and responses to cardiovascular challenges, such as changes in blood pressure, in normal sheep and sheep with heart failure before and after selective vagal stimulation. Confirm site of injection and expression of optogenetic channels. Techniques expected to be mastered during this honours project include – chronic recordings of cardiovascular variables in conscious large animals, quantitative immunohistochemistry, data analysis and statistical methods. There is the potential for publication for motivated students.

Project supervisor
Dr Lindsea Booth

Project co-supervisor
Dr Song Yao and Prof Clive May

- Honours

CLARK GROUP

Contact: **Dr. Mike Clark**

Email: **michael.clark@unimelb.edu.au**

Location: **Kenneth Myer Building**

Weblink: **https://biomedicalsciences.unimelb.edu.au/sbs-research-groups/anatomy-and-neuroscience-research/clark-lab**

Our research sits at the intersection of genomics and neuroscience, utilising a number of genomic approaches to investigate gene expression and function in the human brain and in neuropsychiatric disorders. We are investigating how the expression and splicing of risk genes (both protein coding and noncoding) can change to create disease risk and how detecting these changes can help us understand what causes neuropsychiatric disorders and identify novel treatment targets. A second interest of our research is to develop novel sequencing methods. Recently we have focused on Nanopore sequencing, a technology that can sequence both DNA and native RNA. We are applying Nanopore sequencing to many research questions and developing novel applications for this technology.

Project: Neuropsychiatric disease gene characterisation with Nanopore sequencing

Schizophrenia, bipolar disorder and depression are prevalent and often debilitating mental health disorders with a strong genetic component underlying disease risk. Limited progress has been made in treating these disorders in recent decades, as we still don't have a good understanding of their molecular causes. Many sites in our DNA have been identified that confer disease risk, however, lagging the identification of risk loci is an understanding of which genes are involved and how changes in their expression and splicing confer disease risk. This project will utilize Nanopore sequencing, a ground-breaking new technique, to decipher the expression and splicing patterns of neuropsychiatric risk genes in human brain and stem cell models of brain development. The opportunity exists to perform the sequencing and/or conduct analysis of the expression data. Together this will provide an unrivalled resource for understanding the expression and isoform profiles of neuropsychiatric disease risk genes, knowledge that is critical in order to translate genetic findings into a better understanding of disease pathology and identify potential treatment targets.

Project supervisor
Dr Michael Clark

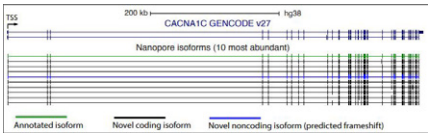
- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: The role of gene isoforms in human brain development

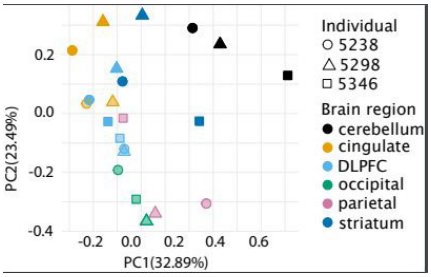
Human brain development is an exquisitely complex process, which is tightly controlled by networks of gene products. Almost all human genes make multiple RNA products (known as isoforms). While current technologies allow the measurement of which genes are active in the developing brain, until now we lacked the ability to resolve the repertoire of gene isoforms and understand their functional roles. We will achieve this by combining single cell RNA sequencing (scRNA-seq), which profiles expression in single cells, with long-read Nanopore sequencing, an emerging technique we have demonstrated has great potential for characterising isoform expression. To examine gene isoforms in the developing brain we will differentiate cortical neurons and cerebral organoids from stem cells, two cutting-edge models of human brain development, which recapitulate early in-vivo human brain development. The knowledge gained from this project will begin to illuminate the role of gene isoforms in brain development and form a foundation for understanding how gene isoforms regulate brain cell functions and fates. The opportunity exists to focus on either the lab side or the computational analysis side of this project.

Project supervisor
Dr Michael Clark

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science



Nanopore sequencing of schizophrenia and bipolar disorder risk gene CACNA1C identifies many novel gene isoforms.



CANCA1C expression variation between human brain regions.

FLETCHER GROUP

Contact: **Prof. Erica Fletcher**

Email: **elf@uniemlb.edu.au**

Location: **Department of Anatomy & Neuroscience**

Weblink: **https https:// biomedicalsciences.unimelb.edu.au/sbs-research-groups/anatomy-and-neuroscience-research/visual-neuroscience**

Retinal diseases are a major cause of blindness in the Western world. There are few successful treatments currently available, largely because the underlying mechanisms of disease are not well understood. The Visual Neuroscience laboratory investigates these underlying disease mechanisms using pre-clinical models and also explores potential mechanisms in individuals with potentially blinding conditions. We are currently studying two broad classes of retinal diseases: 1. Retinal degenerations 2. Retinal vascular disease and oedema.

Project: Pharmacological and laser therapies for age related macular degeneration

Age related macular degeneration (AMD) is a major cause of vision loss in the older community. There are currently no specific treatments for preventing late stage AMD or slowing the progression of the disease to the later vision threatening forms. In this project we will characterise morphological and functional changes in the eye of a pre-clinical model of AMD and test novel pharmacological and laser therapies to ameliorate these changes. This project will involve the use of wide-ranging techniques such as assessment of visual function, immunohistochemistry and molecular biology. Ultimately, this study will help to answer whether novel pharmacological or laser therapies can be used as a preventative treatment for AMD.

Project supervisor
Dr Kristan Vessey

Project co-supervisor
Dr Andrew Jobling
Prof Erica Fletcher

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

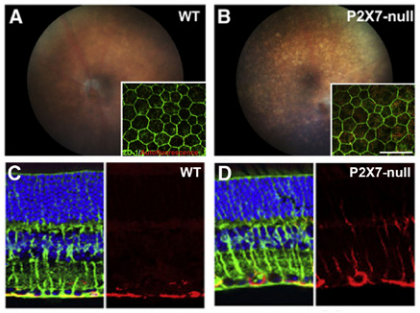
Project: The mechanisms involved in diabetic retinopathy and macular oedema

The retina is highly susceptible to damage arising from the high glucose concentrations present during diabetes. Individuals with type I and II diabetes often develop retinopathy (a vascular pathology) and oedema (fluid-induced swelling). Both these pathologies lead to the development of potentially blinding conditions. The development of macular oedema is thought to involve a specialist neuronal support cell called the Müller glia. Using preclinical models, this project will use in vivo imaging techniques, live cell imaging, immunohistochemistry, and molecular biology to examine the changes in the maintenance of retinal water movement and subsequent retinal swelling. Understanding these changes is critical to explaining the retinal pathology that develops during diabetes.

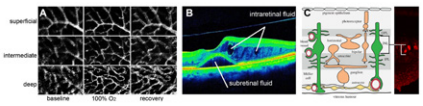
Project supervisor
Dr Andrew Jobling

Project co-supervisor
Prof Erica Fletcher

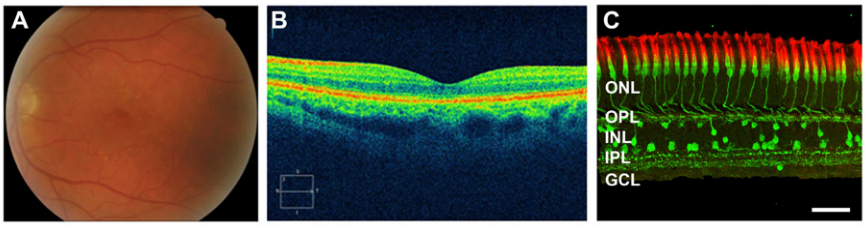
- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science



The pre-clinical model, P2X7-null, shows similar pathology to humans with AMD. Compared to normal (A and C), fundus deposits are visible in the P2X7-null (B), the retinal pigment epithelia are larger (inset B) and the retina shows evidence of gliosis (D, a stress response). We use this model to test new pharmacological and ophthalmic laser treatments. Image modified from Vessey et al 2017.



Retinal capillary vessels can autoregulate their diameter (A) and this is abnormal in diabetes. OCT image showing fluid accumulation in a diabetic retina (B, oedema). Müller cells (green in the diagram in C) are responsible for the maintenance of retinal fluid movement. This project will use fluorescent labelling of Müller cells in retinal slices (C, red) to monitor cell swelling and retinal oedema



Fundus picture of a human retina showing the retinal vasculature (A) and the cross-section OCT image showing the retinal layers (B). Immunolabelling of the human retina showing the different neuronal classes (C), with photoreceptors shown in red and green in the ONL. Modified from Jobling et al, FASEB 2015.

FURNESS GROUP

Contact: **Professor John B Furness**

Email: **j.furness@unimelb.edu.au**

Location: **Department of Anatomy & Neuroscience.**

Weblink: **https://www.ncbi.nlm.nih.gov/pubmed?term=(Furness%20JB%5BAuthor%5D)%20OR%20Furness%2C%20John%20B%5BAuthor%5D**

Digestive Physiology and Nutrition Laboratories

The healthy gut communicates with the brain and lives in harmony with the many bacteria it contains. Disorders of gut health lead to diabetes and metabolic disease, inadequate nutrition, pain, nausea, poor digestion, liver disease, and digestive diseases. The digestive Physiology and Nutrition Laboratory is working to develop new approaches to treating bowel diseases through neuromodulation, an exciting new approach in which nerves are stimulated to treat disordered function, through drug development and by unravelling the basic mechanisms essential for digestive health. We are also working to understand the reasons why gastrointestinal functions become disordered when there are pathologies of the central nervous system, such as in Parkinson's Disease.

Project: The gastrointestinal complications of Parkinson's Disease

Parkinson's Disease causes losses in neural control in the digestive system as well as defects in the central nervous system. Loss of neural control of digestive function commonly occurs before central changes are detected.

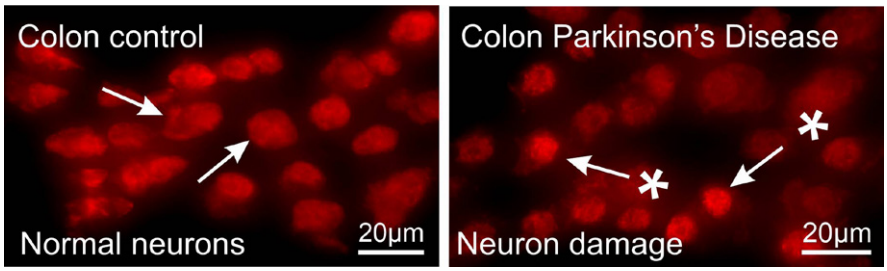
About 70% of people with Parkinson's Disease have digestive problems, most commonly constipation. Importantly for understanding the genesis of Parkinson's Disease, the digestive disorders often precede the motor dysfunction. The constipation could arise from disorders in the central nervous system or from disorders in the enteric nervous system.

In this project, mice with a human mutation that gives rise to Parkinson's Disease and mice and rats with chemically-induced Parkinson's Disease will be used. Physiological, pharmacological and structural approaches will be used to investigate whether central or enteric pathways are involved.

Project supervisor
Dr Rachel McQuade

Project co-supervisors
Professor John B Furness

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science



Project: Neuro-immune interactions: nerve pathways controlling inflammation in the intestine

This study aims to better understand the nerve pathways that sense inflammation in the intestine and control the innate immune cells that mediate inflammatory reactions in the gut. It will also determine how these nerves change in inflammatory conditions of the bowel both in animals and in humans.

You will use neuronal tracing and molecular techniques to identify and characterize the neurons that project to and control immune cells of the gut. You will also use electrophysiological recordings, immunohistochemical and molecular techniques to study the responses of these neurons and changes in their properties during acute and chronic inflammation of the gut in animal and human tissue from patients with inflammatory bowel disease.

Project supervisor
Dr Martin Stebbing

Project co-supervisor
Professor John B Furness

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: Novel heteromeric receptors in gut control: ghrelin receptors and dopamine receptors working together

Ghrelin is a naturally occurring hormone that had been thought to be a transmitter in the central nervous system (CNS), and some years ago we discovered that ghrelin is a powerful CNS-acting stimulant of defecation in animal models and humans. A striking conclusion from our discoveries is that the strong stimulation of defecation by ghrelin agonists is independent of ghrelin, which we discovered to be absent from the CNS. Our data indicate that the physiological activation of the ghrelin receptor, GhrR, is through dopaminergic transmission acting at a combined GhrR / dopamine (DRD2) receptor, as summarised in the figure below. In this project you will investigating how ghrelin and dopamine receptor agonists act and interact at this receptor complex in biophysical systems, isolated cells, native cells and whole animals.

Project supervisor
Dr Linda Fothergill

Project co-supervisor
Professor John B Furness,
Dr Ruslan Pustovit

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: Novel drugs and receptors for targeting neural control of digestive function

We have made a number of discoveries of new compounds that can modify digestive function and are conducting animal proof of principal experiments that we hope will lead to clinical trials. You will work with a team of researchers to investigate the effectiveness and mechanisms of action of novel pharmacological tools.

This project will provide you with the opportunity to conduct in vivo experiments and to learn much about whole animal physiology. One of the major problems of digestive function is failure of propulsive activity. This arises from a variety of neuro□muscular dysfunctions. The most common result is constipation that afflicts more than 20% of the population, many older Australians and most of those with spinal cord injury. We have discovered a new class of drugs that can potentially be used to treat these conditions and this project will further investigate the mechanisms of action and therapeutic potential of novel compounds.

Project supervisor
Dr Ruslan Pustovit

Project co-supervisors
Professor John B Furness

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: Brain-gut axis: Neural pathways controlling the stomach and their relevance for treatment of gastroparesis

The stomach is the portal to the rest of the digestive tract. It signals to the brain to control food intake and it regulates the supply of ingested nutrients to the rest of the gastrointestinal tract. Its correct functioning is thus essential to health. The main nerve connecting the brain and the stomach, the vagus is accessible for nerve stimulation, and thus is a favoured site for neuromodulation therapy.

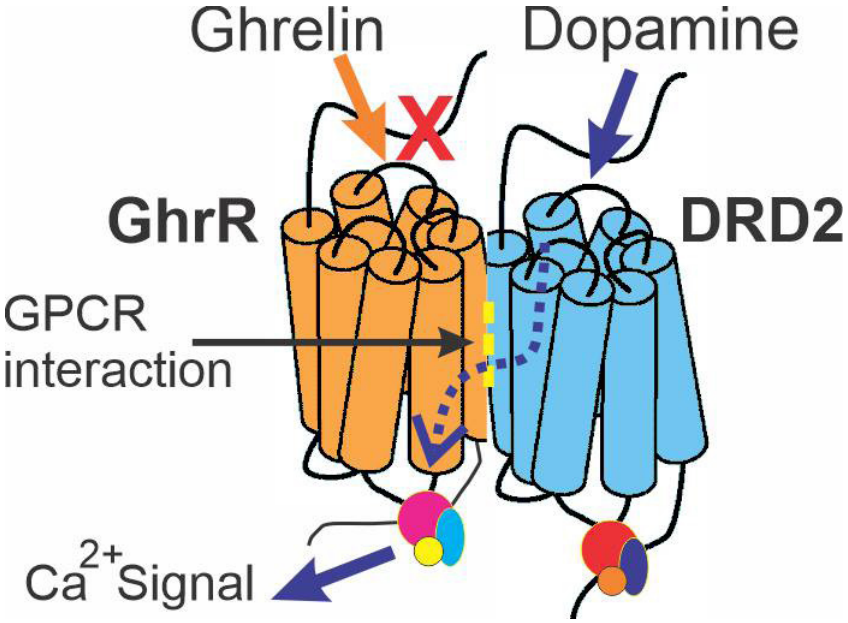
Gastroparesis is a disorder of brain gut signalling in which the brain receives inappropriate signals from the stomach, causing nausea, sometimes vomiting, and inappropriate feelings of gastric fullness. The stomach does not empty properly.

In this project you will investigate gastric control circuits using combinations of techniques, including high-resolution microscopy, multi-label immunohistochemistry, experimental surgery, nerve tracing and gene expression analysis.

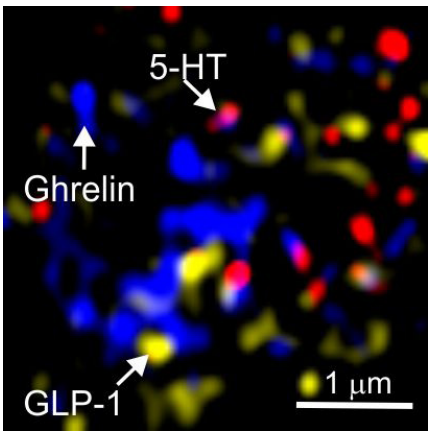
Project supervisors
Professor John B Furness

Project co-supervisors
Dr. Martin Stebbing

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science



Damage to neurons in in the gut wall in an animal model of Parkinsons Disease



Deep inside an enteroendocrine cell: Separate storage of the hormones serotonin (5-HT), ghrelin and GLP-1. Image by super resolution microscopy

Project: Protecting the gut from the damaging consequences of obesity

Obesity is considered to be a global epidemic, with prevalence increasing at an alarming rate in many parts of the world. According to the World Health Organisation (WHO) over 2.1 billion adults were estimated to be obese or overweight in 2016, with worldwide prevalence of obesity doubling since 19801. In Australia, two-thirds of the adult population is obese or overweight.

Damage at the level of the gut in obesity or in response to obesogenic diets has been associated with increased intestinal permeability, often referred to as “leaky gut”6. Strong evidence points to gut leakiness, and consequent entry of endotoxins, as a contributing factor in the initiation of systemic low-grade chronic inflammation and organ damage.

In this project determine whether protection of enteric neurons and the intestinal barrier can improve gut symptoms and impede chronic low-grade inflammation associated with obesity using a clinically approved therapeutic compound.

Project supervisors
Dr Rachel McQuade

Project co-supervisors
Professor John B Furness

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: A stem cell therapy for Hirschsprung Disease

Hirschsprung disease (HSCR) is a congenital enteric neuropathy characterised by the lack of enteric neurons in the distal bowel, which results in a loss of propulsive motility and life-threatening constipation. Without surgical removal of the defective bowel, the infant dies. Current surgical intervention, while life-saving, frequently results in chronic, long-term complications, including constipation, faecal soiling, and associated psychosocial problems Consequently, alternative treatments are needed.

Our studies have shown that following transplantation into the bowel, *endogenous* enteric neural progenitors give rise to new neurons that are electrically active, integrate into the ENS circuitry and functionally innervate the gut muscle. We have embarked on a program to rescue rats from certain death by bypassing the defective bowel, restoring function by stem cell therapy and then re-joining the bowel.

In this project you will participate in the rescue of Hirschsprung rats and you will evaluate recolonization using structural and functional methods.

Project supervisors
Dr Lincon Stamp

Project co-supervisors
Professor John B Furness

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: A stem cell therapy to reverse the effects of spinal cord injury

Spinal cord injury results in loss of control over limb function, causing paraplegia or tetraplegia. Bowel dysfunction (constipation associated with overflow fecal incontinence) is a further debilitating consequence of most spinal cord injuries. Loss of bowel control means most spinally injured people are incontinent and unable to make voluntary bowel movements. A significant number of spinally injured people become socially reclusive because of the embarrassment of fecal incontinence.

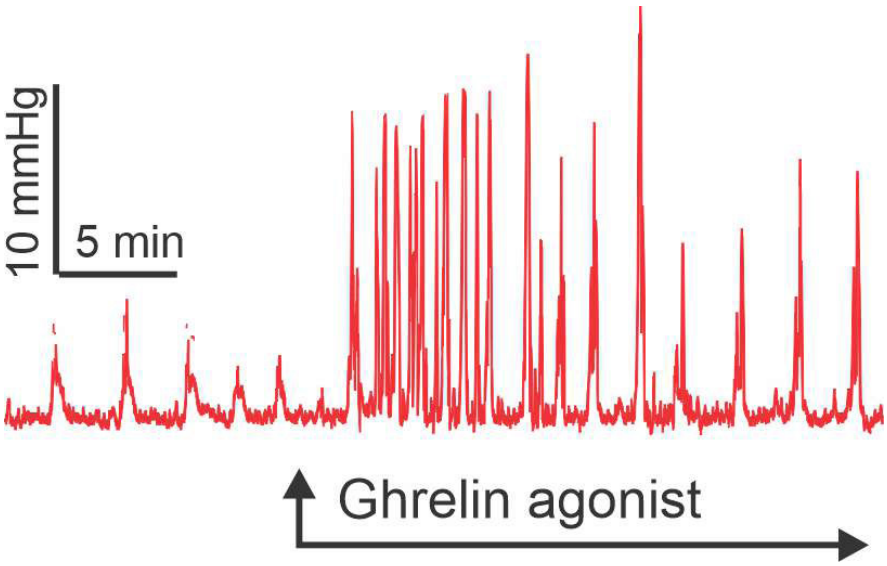
In recent years there has been a degree of success with the use of stem cells to restore spinal cord connection in animals and humans. Mature neurons of the enteric nervous system have a greater plasticity than mature neurons of the central nervous system. Thus, after lesioning in mature animals, enteric neurons regrow and form appropriate functional connections.

In this project you will investigate whether enteric neurons, or enteric neurons plus mesenchymal stem cells, enhance spinal cord repair, and bowel and hind-limb control.

Project supervisors
Professor John B Furness

Project co-supervisors
Dr Lincon Stamp

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science



Stimulation of propulsive activity in the colon by a ghrelin agonist. This record is from proof of principle experiments in animals aimed at translation to therapy

Project: Food entrainment of circadian rhythms

The daily rhythms of sleep, wakefulness, physical activity and eating (circadian rhythms) are coupled to good health. Such rhythms can be set and entrained by light (central clock) or by timed food intake (influencing digestive system rhythms and peripheral clocks). Rhythm disruption by irregular meals, changes in diet, shift work or travel between time zones negatively impacts the functions of various organs and thus our overall health. Despite the importance of circadian rhythms, inadequate knowledge of the baseline circadian rhythmicity in peripheral tissues, the communication pathways for rhythm synchronization, and the potential sex differences holds back understanding of basic mechanisms relevant to health and its disruption.

In this study you will investigate how changed feeding times disrupts circadian rhythms and the expression of nutrient transporters and nutrient handling.

Project supervisors
Dr Lalita Oparija

Project co-supervisors
Professor John B Furness

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: Aptamers: developing a novel technology for hormone measurement

Currently, hormone measurements are made by drawing a blood sample, that is then placed in a detection device, or is sent to a pathology laboratory for analysis. Sending samples to a laboratory means that the result is not known until after the patient has left the clinic, with delays usually being several days.

We intend to develop an entirely new technology, which is called aptamer technology. An aptamer is a chemical that generates an electrical or optical signal when it binds to a hormone. Aptamers can record hormone release in real-time. The electrical or optical signal is transmitted to a smart device and wirelessly communicated to a phone or computer.

We will begin by applying this new technology to the measurement of the stomach hormones, serotonin and ghrelin. In future it will be possible to apply the technology to the measurement of other hormones.

Project supervisors
Dr Linda Fothergill

Project co-supervisors
Professor John B Furness

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

GORDON GROUP

Contact: **Dr Sarah Gordon**

Email: **sarah.gordon@florey.edu.au**

Location: **Florey Institute of Neuroscience and Mental Health**

Presynaptic dysfunction in neurodevelopmental disorders. Neurodevelopmental disorders are a devastating group of conditions characterised by developmental impairments, which usually manifest in infants and children. These disorders can result in a broad range of deficits, including learning delay and intellectual disability, problems with muscle control and movement, and behavioural and emotional issues.

In severe cases the affected individuals may require lifetime care and/or have a reduced life expectancy. Gene technology is now enabling the identification of many novel causes of neurodevelopmental disorder. This provides a new starting point for understanding the relationships between specific genetic mutations, brain function and development, cognition, and mental health.

There is growing evidence that the machinery that controls the release of neurotransmitters is compromised in a range of neurodevelopmental disorders, including intellectual disability, epilepsy, and autism spectrum disorders. We have recently identified the first human mutation in synaptotagmin-1 (Syt1), in a child with a severe neurodevelopmental disorder. The child harbouring this mutation displayed profound intellectual disability, delayed motor development, and severe neurophysiological disturbance, but MRI revealed no structural brain abnormality. This mutation (I368T) occurs in a highly conserved residue in Syt1.

We examined the effect of I368T Syt1 on presynaptic activity and found that the presence of this mutant variant of Syt1 in neurons resulted in altered synaptic vesicle recycling dynamics. We have now identified a further 5 mutations in Syt1, in individuals who have symptoms that largely overlap with our index case, but with differing degrees of severity.

Project: Investigate how mutations in Syt1 affect the synaptic vesicle cycle, and whether these effects are treatable

This project will examine whether all Syt1 mutations cause the same alterations to neurotransmitter release dynamics, thereby determining the molecular mechanisms underlying neurodevelopmental disorders in individuals harbouring these mutations. Intriguingly, mutations in the related protein, synaptotagmin-2, cause a neuromuscular disorder which is treatable. We will investigate whether pharmacological intervention with this same drug can at least partially overcome some of the deficits caused by mutations in Syt1.

This project will implement a variety of techniques, including molecular biology, biochemistry, primary neuronal cell culture, fixed immunofluorescence imaging and live-cell fluorescent imaging, giving students the opportunity to master a range of key transferrable skills.

Project supervisor
Dr Sarah Gordon

- Ph.D.
- Honours
- Master of Biomedical Science

Project: Investigate how alpha synuclein regulates the synaptic vesicle cycle and neurotransmitter release

Alpha synuclein has been proposed to modulate various aspects of the synaptic vesicle cycle. Importantly, it controls the presynaptic targeting of a key synaptic vesicle protein, synaptobrevin II, which is crucial for neurotransmitter release. This project will determine how alpha synuclein regulates the localisation and function of synaptobrevin II and the implications this has for synaptic vesicle dynamics and neurotransmitter release.

Project supervisor
Dr Sarah Gordon

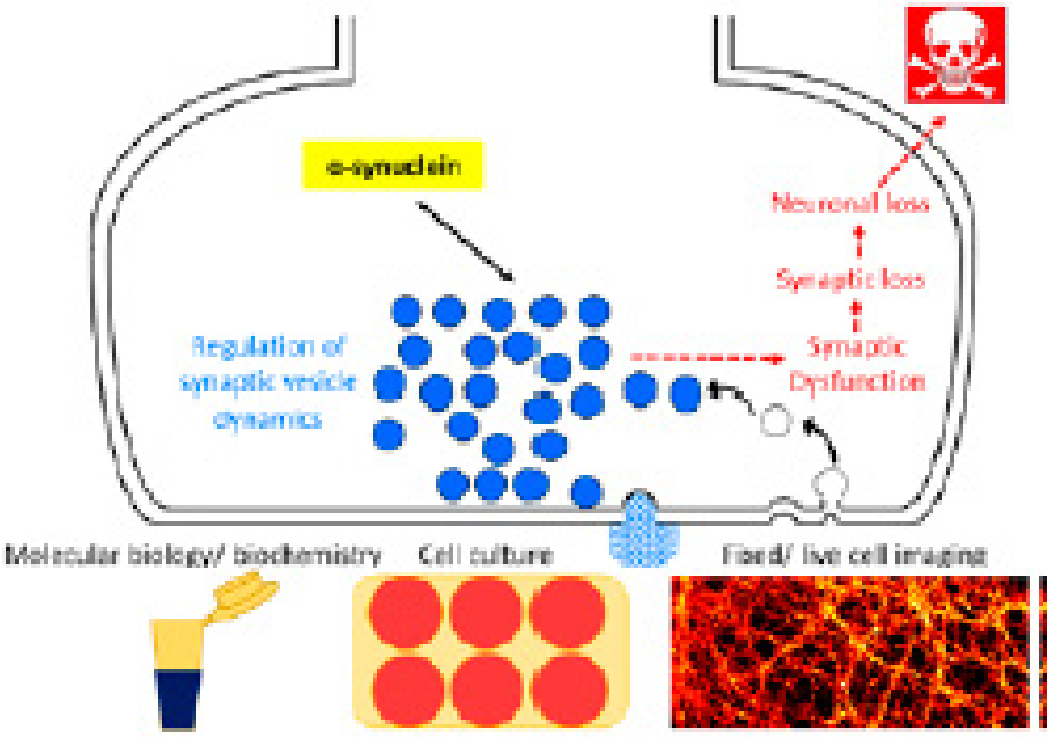
- Ph.D.
- Honours
- Master of Biomedical Science

Project: Investigate how phosphorylation controls the function of alpha synuclein at nerve terminals

We have recently identified novel sites in alpha synuclein that are phosphorylated in an activity-dependent manner. This project will ascertain how phosphorylation at these distinct residues modulates the function of alpha synuclein as a regulator of presynaptic activity.

Project supervisor
Dr Sarah Gordon

- Ph.D.
- Honours
- Master of Biomedical Science



GUNNERSEN GROUP

Contact: **Dr. Jenny Gunnersen**
Email: **jenny.gunnersen@unimelb.edu.au**
Location: **Department of Anatomy & Neuroscience**

The Neuron Development and Plasticity group, led by Jenny Gunnersen, has the broad research goal of understanding how neurons become connected into functional circuits. We investigate the formation of dendritic branches and synapses, the connections between neurons, in development and in disease models. Changes in the number and strength of synaptic connections (plasticity) are vital for the development of effective neuronal circuitry and for learning and memory in the healthy brain. On the other hand, abnormal synapse numbers and activity are defining features of neurological disorders. Learning more about dendrite and synapse development and function in the healthy brain will help us decipher the aberrant molecular pathways responsible for cognitive disorders such as mental retardation, epilepsy, schizophrenia and dementia.

Project: Using knockout mouse models to investigate synaptic pruning

Microglia are sentinels of the brain circuitry involved in “pruning” of weak or inactive synapses during development and monitoring and refining synaptic connectivity in the adult brain. A mechanism for “tagging” unnecessary synapses for removal has been described, however whether a complementary mechanism exists to protect active synapses from being pruned is a major unanswered question. The effect of gene knockout on putative pruning regulators will be determined.

Project supervisor
Dr Jenny Gunnersen

- Honours
- Masters
- Ph.D

Project: Is the ‘shed’ form of Sez6 proteins responsible for their synapse-promoting effects?

Certain proteins, including Sez6 family proteins, can be located either on the surface of neurons or shed from the surface of neurons by the actions of particular proteases. Secreted proteins and shed forms of transmembrane proteins are then able to act on nearby neurons to influence their growth and the formation of synaptic connections. This project will compare the effects of secreted and shed forms of Sez6 family proteins on the growth of neuronal arbors (dendrites, axons) and synaptogenesis.

Project supervisor
Dr Jenny Gunnersen

Project co supervisor
Dr Kathryn Munro

- Honours
- Masters
- Ph.D

Project: Investigating the anti-inflammatory effects of deleting a gene in neurons

Our recent data indicate that Sez6 proteins are linked to inflammation. Firstly, Sez6 levels are elevated in cerebrospinal fluid from surgical patients with chronic, painful inflammatory conditions, compared to those in patients attending the hospital emergency department for acute conditions. Secondly, quantitative proteomics of brain extracts from mice lacking Sez6 family proteins indicates that pro-inflammatory signalling pathways are less active in the absence of Sez6 proteins. This project will use biochemical and histochemical methods and flow cytometry to investigate these links.

Project supervisor
Dr Jenny Gunnersen

- Honours
- Masters
- Ph.D

HANNAN GROUP

Contact: **Prof. Anthony Hannan**
Email: **anthony.hannan@florey.edu.au**
Location: **Florey Institute of Neuroscience and Mental Health**

Weblinks h**ttps://www.florey.edu.au/science-research/research-teams/epigenetics-and-neural-plasticity-laboratory**

https://www.ncbi.nlm.nih.gov/pubmed/?term=hannan+aj

The Epigenetics and Neural Plasticity Laboratory at the Florey Institute of Neuroscience and Mental Health.

We explore how genes and the environment combine via experience-dependent plasticity in the healthy and diseased brain. Our research includes models of specific neurological and psychiatric disorders which involve cognitive and affective dysfunction, investigated at behavioural, cellular and molecular levels so as to identify pathogenic mechanisms and novel therapeutic targets. Most recently, this has included studies of intergenerational and transgenerational epigenetic inheritance.

We investigate how genetic and environmental factors combine to cause specific cognitive and affective disorders, including Huntington's disease, dementia, depression, anxiety disorders, schizophrenia and autism spectrum disorders. Our research also 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 can modulate 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, proteomics and metabolomics. We are also exploring the concept of 'enviromimetics', therapeutics that mimic or enhance the beneficial effects of cognitive stimulation and physical exercise.

Project: Targeting gut microbiota to understand and therapeutically modulate pathogenesis in Huntington's disease

Huntington's disease is a neurodegenerative disorder involving complex symptomatology, including cognitive deficits (culminating in dementia), psychiatric symptoms (particularly depression) and motor deficits (including chorea). There are no disease-modifying therapies available for this devastating disease, which progresses over 10-20 years before killing patients. Recent years have witnessed the rise of the study of gut microbiota (the billions of bacteria and other microorganisms living in the gastrointestinal tract) as a major research topic for complex central nervous system disorders. This revolution in biomedical research has revealed that, in addition to the trillion or so cells in each of our bodies, we have over a trillion microbes (mainly bacteria) living in and on our bodies, particularly the gut. We were recently the first to discover dysbiosis (altered gut microbiome profile) in Huntington's disease. This was achieved via DNA sequencing using fecal samples from a transgenic mouse model of Huntington's disease (R6/1 mice).

This project aims to study new pharmacological and environmental interventions to delay the onset of Huntington's disease in this transgenic mouse model, via experimental manipulations of gut microbiome composition. We will investigate impacts on the dementia and depression-like behaviours, as well as the movement disorder. This project will use environmental and pharmacological modulation, cognitive and behavioural tasks, as well as cellular and molecular approaches, including genetics, genomics and bioinformatics tools.

Project supervisor
Professor Anthony Hannan

Project co-supervisor
Dr. Carolina Gubert,

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: Intergenerational molecular, cellular and behavioural effects of a Western-style paternal diet via epigenetic inheritance

Western diets (WD) with a high proportion of saturated fats and refined sugars have a considerable influence on the development of overweight and obesity. Critically, worldwide obesity tripled between 1975 and 2016. Currently, 1.9 billion adults are overweight, with over 650 million of them being obese. 381 million children and adolescents are affected by overweight or obesity. Obesity-associated comorbidities such as cognitive impairment and anxiety are increasing public health burdens that have particularly gained prevalence in children. Since there is evidence that parental obesity is associated with childhood obesity and its comorbidities via epigenetic programming, it is of utmost importance to unveil the underlying mechanisms as well as the exact consequences parental obesity has on the offspring in order to better understand and prevent the processes that are involved.

The study of how fat and sugar influence sperm RNA and DNA as well as anxiety-related, cognitive, and social behaviours in the offspring is still in its infancy. In particular, the growing numbers of obese children and adolescents call for a detailed investigation of how the exposure to an unhealthy diet in early phases of life can affect spermatogenesis as well as intergenerational and transgenerational epigenetic inheritance. The period of adolescence, the transition time from childhood to adulthood, is a critical phase for the developing organism. During this time, substantial remodelling of the brain occurs in response to hormonal and physical changes. Hence, the brain is particularly sensitive to external influences, such as nutrition.

Daily consumption of WD during adolescence may lead to physiological, behavioural, and cognitive impairments as well as alterations in sperm non-coding RNA levels and DNA methylation. Although there are recent indications that paternal obesity can epigenetically affect some aspects of the offspring phenotype, the mechanisms are unclear.

This project aims to study the impact of dietary interventions on male laboratory mice and their female and male offspring. To achieve this goal, fathers are provided free access to a Western-style high-fat/high-sugar diet, leading to significantly increased body weights compared to mice fed a control diet. A variety of behavioural tasks as well as cellular/molecular approaches will then be used to gain a comprehensive picture of the offspring endophenotypes. We will also using cutting-edge epigenetic approaches to elucidate the modulation of the sperm epigenome and offspring development, physiology and metabolism. Due to the high translational value of this project, the results will be crucial to our understanding of the of the epigenetic intergenerational impacts of 'junk food' on molecular and cellular mediators of brain function, cognition and behaviour.

Project supervisor
Prof. Anthony Hannan

Project co-supervisor
Dr Carina Bodden

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: Targeting gut microbiota in an animal model of schizophrenia: new hope for translational therapeutics

Importantly, 60% of schizophrenic patients are treatment-resistant and this subpopulation has the highest levels of impaired functioning and rates of hospitalization. Interestingly, chronic gastroenterological issues such as gut inflammation are common co-morbid symptoms of schizophrenia. The potential role for the microbiome in schizophrenia pathogenesis had been highlighted, which is now established to be dysregulated in schizophrenic patients compared to healthy controls. Thus, the collective evidence indicates a crucial role for the gut microbiome in schizophrenia pathogenesis, but the potential implications for treatment-resistant patients remains to be investigated. This proposal will explore the status of the gut microbiota in a well-studied mouse model of schizophrenia, followed by an exploration of how direct modulation of gut microbiota influences the behavioural response. Our findings will inform the role of gut microbiota dysbiosis in schizophrenia, uncovering new aspects of schizophrenia pathology that could lead to novel therapeutic targets to improve the treatment of the cognitive, psychiatric and social symptoms. More broadly, there could also be implications for improving therapeutic approaches for other psychiatric disorders. This project will use microbial, environmental and pharmacological modulation, cognitive and behavioural tasks, as well as cellular and molecular approaches, including genetics, genomics and bioinformatics tools.

Project supervisor:
Prof. Anthony Hannan

Project co-supervisor
Dr Carolina Gubert

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

HIME GROUP

Contact: **Prof Gary Hime**

Email: **g.hime@unimelb.edu.au**

Location: **Department of Anatomy & Neuroscience**

Weblinks: **https://www.ncbi.nlm.nih.gov/pubmed/?term=hime+gr**

https://biomedicalsciences.unimelb.edu.au/sbs-research-groups/department-of-anatomy-and-neuroscience/stem-cell-genetics

The Hime groups studies regulation of organ development and regeneration in Drosophila and vertebrate tissues. Many differentiated but renewable cell types are derived from relatively small populations of dedicated precursors, or stem cells. The ability to replenish differentiated cells depends on the continued survival and proliferation of their respective stem cell populations. If we are to realise the goals of re-programming tissue differentiation, growing organs for transplantation *in vitro*, regeneration of damaged organs *in vivo* and targeted effective treatments for cancer it is essential that we understand the molecules and mechanisms that stem cells utilise for renewal and differentiation.

Project: Analysing the role of transcriptional regulators in Drosophila and mouse stem cells

We have shown that transcriptional regulators of epithelial to mesenchymal transition are required in diverse stem cell populations. This role has been conserved through evolution of animals as these proteins can be found in stem cells from *Drosophila* to mouse. This project involves using CRISPR and genetically modified *Drosophila* or mouse intestinal organoid cultures to identify how these proteins regulate stem cell numbers and control the production of differentiated progeny cells. See Horvay et al (2015), Voog et al (2014) and Horvay et al (2011).

Project supervisor
Prof Gary Hime

Project co-supervisor
A/Prof Helen Abud (Monash University)

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: Identification of novel regulators of stem cell differentiation

We have conducted genetic screens which have identified new mutations that affect the ability of *Drosophila* male germline stem cells to differentiate. This project will involve genetic analysis and DNA sequencing to identify genes associated with specific mutations and phenotypic characterization of the mutant to determine the mechanism affecting stem cell differentiation. See Dominado et al (2016) and Monk et al (2010).

Project supervisor
Prof Gary Hime

Project co-supervisor
Dr Nicole Siddall

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

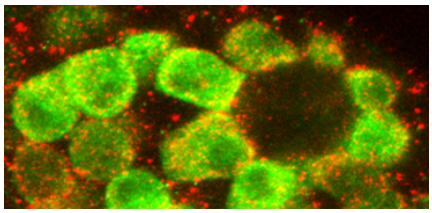
Project: Stem cell competition

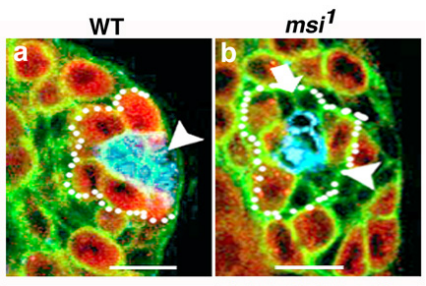
If a mutation in a cell signaling pathway occurs in a stem cell can that cell outcompete other stem cells and result in the entire stem cell pool of an organ being derived from that single cell? What effects might this have on the ability of the stem cell to differentiate and produce functional cells? This project will use the genetic tools available in *Drosophila* to generate single mutant stem cells and follow their progeny. We will assay what proportion of the stem cell pool is generated from the mutant stem cell over time and if the mutant cells can produce functional differentiated progeny.

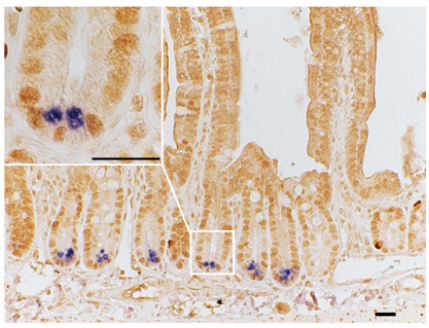
Project supervisor
Prof Gary Hime

Project co-supervisor
Dr Nicole Siddall

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science







Project: How does alternative splicing regulate stem cell maintenance

Regulators of RNA splicing can lead to different isoforms of genes being expressed in stem cells. This project will use genetic methods, immunostaining and confocal microscopy to determine if different splice forms of signalling molecules affect stem cell maintenance and differentiation.

Project supervisor
Prof Gary Hime

Project co-supervisor
Dr Nicole Siddall

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: Drosophila models of human disease

The rapid advances in sequencing of human genomes has identified many variant gene sequences that may be associated with genetic diseases. It can be difficult to unambiguously associate genetic variants with phenotypes without a direct assay. We are using Drosophila to model the effects of genetic variants associated with human disease to determine how the variants affect gene function.

Project supervisor
Prof Gary Hime

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: Transgenerational modification of survival efficacy in the advent of climate change

There are several lines of evidence that parental health is strongly linked to offspring health outcomes. In humans and mammalian models, non-genetic factors established to impact on offspring include traumatic/chronic stress and imbalanced diets. However, metabolic consequences pertaining to thermoregulation are ill-defined. Extreme climate events are becoming more frequent with documented consequences for the reproduction and population sizes of a variety of insects globally. Here, we will use the drosophila model to study how transient exposures to temperature spikes can cause a transgenerational shift in the survival probability of subsequent generations. Using distinct genetic strains with differential heat resistance (Stonehouse, Hime & Pang, unpublished), we seek to identify precise molecular mechanisms regulation in form of transgenerational inheritance. We will also be investigating how heat stress impacts on the male reproductive system to initiate the transgenerational response.

Project supervisor
Prof Gary Hime

Project co-supervisor
Dr Terence Pang (Florey)

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Key publications:

Dominado N, La Marca JE, Siddall NA, Heaney J, Tran M, Cai Y, Yu F, Wang H, Somers WG, Quinn LM* and Hime GR* (2016) Rbf regulates Drosophila spermatogenesis via control of somatic stem and progenitor cell fate in the larval testis. *Stem Cell Reports*, 6:1152-1163

Horvay K, Jarde T, Casagranda F, Perreau VM, Haigh K, Nefzger CM, Akhtar R, Gridley T, Berx G, Haigh JJ, Barker N, Polo JM, Hime GR* and Abud HE* (2015) Snai1 regulates cell lineage alLocation: and stem cell maintenance in the mouse intestinal epithelium. *EMBO Journa*l, * joint senior authors, 34(10):1319-35

Voog J, Sandall SL, Hime GR, Resende LP, Loza-Coll M, Aslanian A, Yates JR 3rd, Hunter TC, Fuller MTC, Jones DLC. (2014) Escargot restricts niche cell to stem cell conversion in the Drosophila testis. *Cell Reports* 7:722-734

Horvay K, Casagranda F, Gany A, Hime GR and Abud HE (2011) Wnt signalling regulates Snai1 expression and cellular localisation in the mouse intestinal epithelial stem cell niche. *Stem Cells and Development*, 20(4): 737-745

Monk AC, Siddall NA, Volk T, Fraser BA, Quinn LM, McLaughlin EA and Hime GR. (2010) The RNA-binding protein HOW is required for stem cell maintenance in the testis and for the onset of transit amplifying divisions. *Cell Stem Cell*, 6: 348-360

Siddall NA., McLaughlin E, Marriner NL. and Hime GR. (2006) The RNA-binding protein Musashi is required intrinsically to maintain stem cell identity. *Proc. Natl. Acad. Sci. U.S.A.* 103:8402-8407.

Hogan Group

HOGAN GROUP

Contact: **Prof. Ben Hogan**
Email: **ben.hogan@petermac.org**
Location: **Peter MacCallum Cancer Centre**

The Hogan group investigates the development of lymphatic vasculature and the blood brain barrier, which play important roles in the metastatic spread of cancer and vascular disease. We use zebrafish and mice as model systems to study fundamental processes in the developing embryo. Current projects are focussed on signalling and transcriptional mechanisms that control lymphangiogenesis. We are also using large-scale genetic and genomic approaches to discover new genes essential for development of the blood brain barrier. In addition, we are interested in developing imaging tools to visualise key cell signalling events in real time in vascular development and disease models.

Zebrafish models of vascular disease: lymphatic malformation

Lymphatic malformation (also known as lymphangioma) is a rare childhood disease caused by uncontrolled proliferation of the lymphatic endothelium. These malformations are typically present at birth, or soon after, and are largely treated with surgery. The genetic causes of lymphangioma remain to be fully understood but somatic mutations in PIK3CA, impacting the AKT-mTOR pathway, have emerged as causative in many cases. The project will generate genetic, inducible, models of lymphangioma in zebrafish and attempt to generate CRISPR-induced somatic mutation models. These will drive vascular malformation by expression of mutant PIK3CA expression. Phenotype will be assessed with molecular markers and confocal imaging. The models generated will ultimately be used to assess the efficacy of a series of candidate therapeutic molecules.

Project Supervisor:
Prof Ben Hogan

Project Co-supervisor:
Dr Kazuhide Okuda

- Honours
- Master of Biomedical Science

Project: Cell fates and cell states: analysis of enhancer dynamics during angiogenesis and lymphangiogenesis

Cellular fates are regulated by key transcription factors during vascular development, angiogenesis and lymphangiogenesis. How transcription factors drive dynamic changes in vessel growth, dynamic enhancer activities, dynamic cell behaviours and cellular heterogeneity in the growing vasculature, remains to be determined. Live imaging reporters of enhancer activity during zebrafish vascular development offers a unique opportunity to approach these fundamental questions. This project will take advantage of a large-scale dataset recently generated in the Hogan lab using single cell ATAC-seq data to assess the developing vasculature of the zebrafish embryo. The project will clone and assess functional enhancers that are lineage specific, evolutionarily conserved and candidate elements that may control dynamic cell behaviours during new vessel formation. Molecular approaches *in vivo* will be coupled with bioinformatics studies to predict of key functional regulators.

Project Supervisor:
Prof Ben Hogan

Project Co-supervisor:
Dr Lizzie Mason

- Honours
- Master of Biomedical Science

Project: The Hippo pathway and Yap1 in vascular growth control in development and disease

Lymphatic vessels play roles in the drainage of tissue fluid, trafficking of immune cells and the metastatic spread of cancer. Inhibiting or enhancing the development of new lymphatic vessels has therapeutic potential in a host of diseases. We recently described a role for Yap1 in lymphangiogenesis in the zebrafish embryo, in response to Vegfc/Vegfr3 signalling. This work, and work from others, has confirmed that the Hippo pathway and Yap are central in vascular growth during development, yet how they control angiogenesis, lymphangiogenesis, vessel proliferation and vascular network patterning remains far from understood. This project will use molecular genetics, biochemical approaches and live imaging of cellular behaviours in zebrafish, mice and cultured human cell lines to understand the mechanistic control of vascular development by the Hippo pathway and Yap. The project will generate novel CRISPR mutants, new transgenic lines and may utilise single cell sequencing of developing vasculature. We will also investigate metabolic control by the pathway in vascular growth and development. Finally, the project will have the opportunity to assess tumour vasculature and pathological settings.

Project Supervisor:
Prof Ben Hogan

Project Co-supervisor:
Dr Andrew Cox

- Honours
- Master of Biomedical Science

IVANUSIC GROUP

Contact: **Assoc. Prof Jason Ivanusic**

Email: **j.ivanusic@unimelb.edu.au**

Location: **Department of Anatomy & Neuroscience**

Weblinks: **https://biomedicalsciences.unimelb.edu.au/sbs-research-groups/anatomy-and-neuroscience-research/pain-and-sensory-mechanisms**

Pain associated with skeletal pathology or disease puts a significant burden (both in terms of quality of life and cost) on individuals, society, and the health care systems worldwide. Pain is the major reason why most of these patients present to the clinical environment. Opioids and non-steroidal anti-inflammatory drugs (NSAIDs) are used to treat mild to severe bone pain, but therapeutic use over long periods required to treat chronic or intractable bone pain is limited by severe and undesirable side-effects. There is a clear need to identify alternative approaches for the management of skeletal pain. Our aim is to explore how peripheral sensory neurons that innervate bone contribute to the experience of skeletal pain, and how their function is affected by skeletal pathology and disease.

Project: Molecular mechanisms that contribute to skeletal pain

Skeletal pain is transmitted by two classes of peripheral nociceptors. Aδ nociceptors are medium-diameter myelinated neurons that transmit fast, intense pain, of the sort experienced in fracture and breakthrough cancer pain. C nociceptors are small-diameter unmyelinated neurons that encode slow, burning pain, of the sort experienced in cancer and osteoarthritis. A number of ion channels and receptors are emerging as important modulators of the activity of peripheral bone nociceptors. Identifying these regulators of nerve activity and better understanding their role in generation of bone pain could open up avenues for development of tools to selectively manipulate pain originating from bone.

In this project, we will use a variety of techniques and animal models to explore roles for different ion channels and receptors in generating and/or maintaining skeletal pain. We are currently interested in modelling experimental inflammation of the bone marrow, osteoarthritis and bone cancer induced skeletal pain. Depending on the particular ion channel or receptor that is being explored, students can expect to gain experience in working with animal models of skeletal pathology, an in vivo electrophysiological bone-nerve preparation, neuroanatomical tracing and immunohistochemistry, small animal handing, anaesthesia, surgery and/or dissection.

Project supervisor
Associate Professor Jason Ivanusic

Project co-supervisor
Dr Michael Morgan

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

KEAST-OSBORNE GROUP

Contact Name: **Professor Janet Keast and Dr Peregrine Osborne (co-lab heads)**

Email address: **jkeast@unimelb.edu.au peregrine.osborne@unimelb.edu.au**

Location: **Dept Anatomy and Neuroscience, Medical Building**

Voiding and reproduction are important human functions that require complex reflexes to be coordinated at behaviourally appropriate times. Our goal is to help develop neuromodulation and other therapies to treat clinical conditions affecting these complex functions. This includes studies to provide high resolution maps and computational models of these neural circuits in rodents and human specimens, define how these peripheral, spinal and brain circuits develop; and how they might be manipulated to provide clinical treatments in diverse medical specialties including urology, gastroenterology, sexual medicine, neurology and pain medicine. We are supported by the US National Institutes of Health (NIH) SPARC program and have also contributed to the NIH-funded GenitoUrinary Development Molecular Anatomy Project database (GUDMAP).

Project 1: Building components of the connectome for the urogenital nervous system

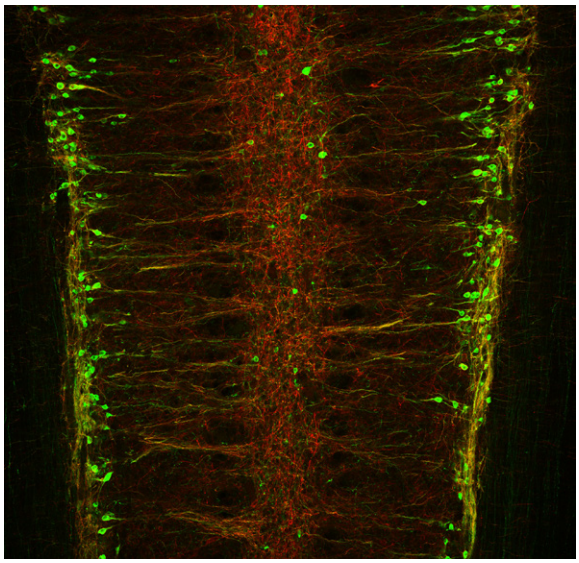
A range of studies are available in this area and are especially suited to students with a strong background in neuroanatomy, neurophysiology or bioengineering. Development of devices to control urogenital function first needs a high-resolution map of neuronal connections with each tissue and region of the urogenital system, its relevant sensory and motor ganglia, the lumbosacral spinal cord and brainstem. Some elements of this map are known but there are many gaps. We are combining tract tracing approaches with combinatorial expression mapping and advanced microscopy (including light sheet microscopy) to precisely map and model connections of distinct nerve types at the macroscopic, mesoscopic and microscopic levels. We are also mapping activity of circuit components using immediate early gene expression patterns after conscious bladder activity, evoked by natural stimulation or activation of a miniaturised device built by our collaborators at the Bionics Institute.

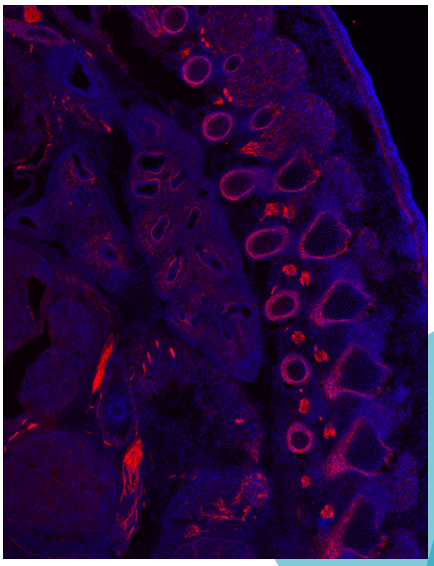
Project supervisors:
Prof Janet Keast and Dr Peregrine Osborne

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project 2: Development of autonomic and nociceptive nerve circuits

A range of studies are available in this area and are especially suited to students with a strong background in developmental biology or neural structures. Urogenital function is regulated by autonomic neurons in the pelvic ganglia (known as the inferior hypogastric plexus in people) and sensory neurons in lumbosacral dorsal root ganglia. In comparison to other parts of the autonomic nervous system, the pelvic ganglia are very unusual. For example, they are very different in males and females, and they continue to be very sensitive to actions of steroids, even in adults. Most unusually, they are mixed sympathetic-parasympathetic ganglia,





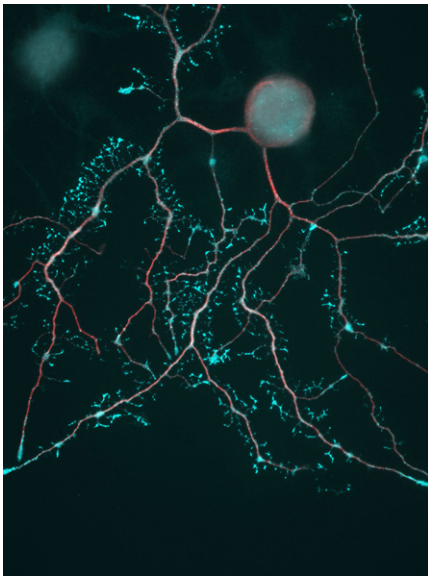
leading to questions of how these ganglia develop, and how their connections with two different regions of the spinal cord (lumbar and sacral) are determined correctly when they first form. Very little is known about how this part of the autonomic nervous system develops and what initiates its sexual dimorphism. These are critical to understanding developmental abnormalities and may also point to mechanisms that can be activated in adults to repair axons after injury. Other projects are available to investigate the unique features of developing sacral nociceptive neurons that are later involved in sexually dimorphic pelvic pain conditions.

Project supervisors:
Prof Janet Keast and Dr Peregrine Osborne

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project 3: Neuroanatomy of human visceral systems

Several studies are available that are especially suited to students with a strong background in visceral anatomy and tissue structure. Although many macroscopic aspects of organ anatomy and innervation are known, there are major gaps in our understanding of the mesoscopic and microscopic structural features of organ innervation and the relevant neural tracts and ganglia that connect the organs with the spinal cord. Much of what is known about organ innervation has been learned from small clinical biopsies or cadaveric samples. These provide limited opportunity for detailed neural characterization or visualization. A particularly poorly understood structure is the inferior hypogastric plexus. This is a large, complex ganglionated p that incorporates the majority of autonomic neurons regulating pelvic organ function and provides the physical route by which most sensory axons reach these organs. This structure is especially vulnerable during pelvic surgery (e.g., prostatectomy), leading to many postsurgical problems relating to voiding, continence or sexual function. These projects will provide excellent opportunities to develop microdissection skills and to apply new tissue clearing, microscopy and neural labeling approaches to map innervation of human lower urinary tract and associated organs (e.g., prostate gland), or their related neural tracts and ganglia. For longer projects, there will also be opportunities to extend studies to several clinical conditions, in collaboration with clinical experts.



Project supervisors:
Prof Janet Keast and Dr Peregrine Osborne

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

LAWRENCE GROUP

Contact: **Professor Andrew Lawrence**

Email: **address:Andrew.lawrence@florey.edu.au**

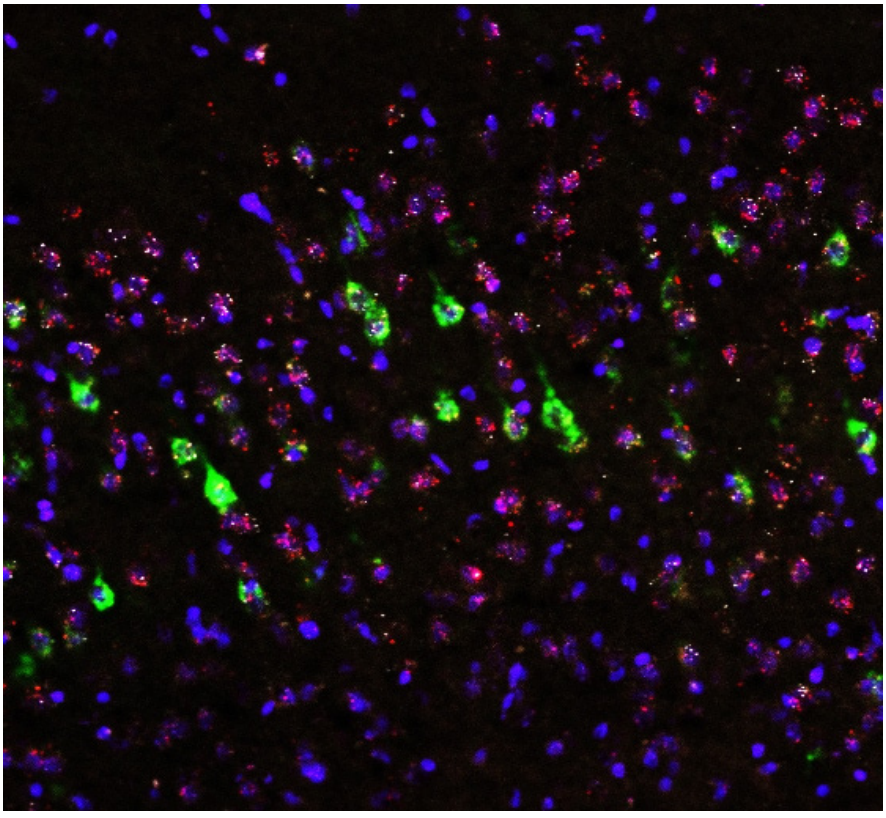
Location: **Florey Institute of Neuroscience and Mental Health**

The Addiction Neuroscience Laboratory at Florey Institute of Neuroscience and Mental Health. Our overarching research aim is to understand the brain mechanisms that drive drug and alcohol-seeking, and relapse to drug-seeking after a period of abstinence. We are also interested in the effects of chronic drug and alcohol intake on cognition and behaviour. Our lab employs a range of different behavioural and molecular techniques to investigate cellular and circuitry changes that occur as a result of exposure to drugs and alcohol, and how these changes may lead to the compulsive behaviour that is characteristic of addiction.

Project: Muscarinic receptors in alcohol-seeking

Despite the major socioeconomic burden, alcohol use disorders (AUDs) remain a major health risk, and current medications are still inadequate to treat both relapse and heavy drinking. Our lab has recently shown muscarinic acetylcholine receptors (mAChR) and nicotinic acetylcholine receptors (nAChRs) undergo adaptations following chronic alcohol consumption in both humans and rodent brains. Further, using selective compounds we have recently confirmed the functional relevance of M4 and M5 mAChRs in regulating voluntary alcohol intake and relapse behaviour in rodents. Therefore, in this study we aim to:

1. Characterise the brain region specific molecular consequences of chronic intermittent alcohol intake on cholinergic receptor expression and function.
2. Examine in rats how brain region specific pharmacological manipulations of muscarinic and nicotinic receptors impact alcohol use / relapse.



Fluorescent In situ hybridisation shows mRNA of M4 (red) and M5 (white) mAChRs are expressed on cells that project from the ventral hippocampus to the nucleus accumbens (as indicated by expression of the retrograde tracer, Cholera toxin B; CTb, green).

This project will utilise a range of molecular and behavioural techniques including operant self-administration, rodent surgery, fluorescent in situ hybridisation, qPCR, microscopy and immunohistochemistry.

Project Supervisor
Dr Leigh Walker

Project co-supervisor
Prof Andrew Lawrence

- Master of Biomedical Science
- Honours

Project: Investigating cocaine and amphetamine regulated transcript (CART) in binge drinking

Alcohol is the leading cause of death globally of people aged 15-49 and is a major socioeconomic burden on Australian society. Alcohol use disorders are an emerging issue in females with rates increasing over 80% in the last 15 years. Current therapeutics fail to adequately address this problem, and sex differences remain understudied. We have recently implicated sex dependent role for the neuropeptide, cocaine and amphetamine regulated transcript (CART) in binge alcohol consumption. However, the regions in which this neuropeptide acts to mediate these behaviours require elucidation.

Therefore, in this study we will:

1. Examine in which brain regions CART neurons are activated by binge drinking in male and female mice using Fos immunohistochemistry and in vivo fiber photometry.
2. Using a genetically-modified mice that allow us to selectively target CART neurons, examine region specific roles of CART via manipulation with DREADDs (designer receptors exclusively activated by designer drugs) during binge drinking.

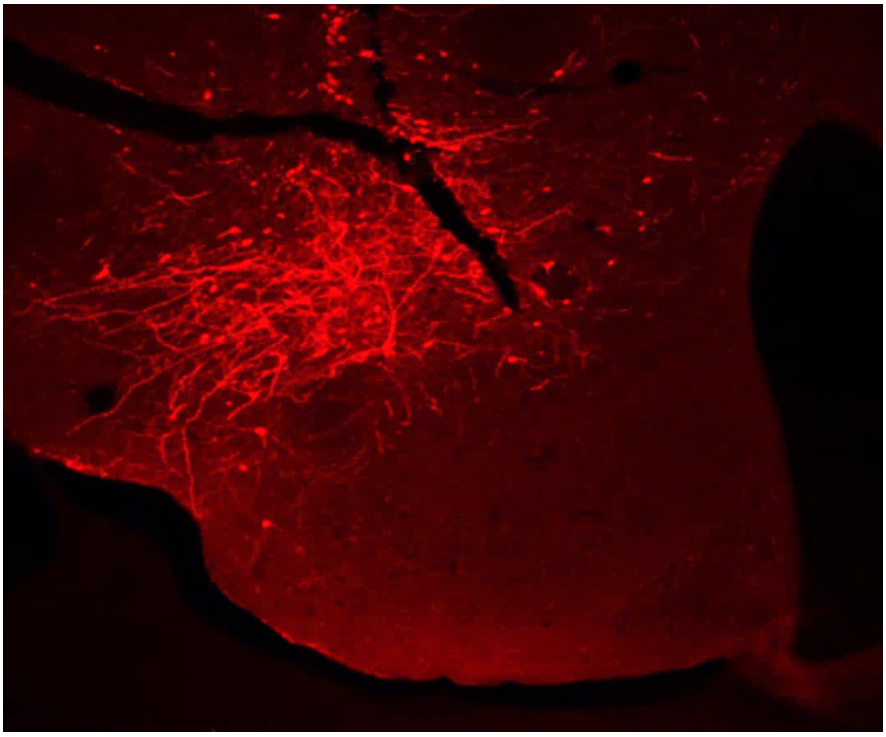
Techniques used in this project include DREADDs, fiber photometry, mouse behaviour, mouse stereotaxic surgery, confocal microscopy and immunohistochemistry.

Project Supervisor
Dr Leigh Walker

Project co-supervisor
Prof Andrew Lawrence

- Ph.D.
- Master of Biomedical Science
- Honours

DREADD receptors inserted specifically into CART cells within the lateral hypothalamus expressing the red fluorescent protein (TdT, red) and a surrogate marker of neuronal activation, Fos (green). Administration of clozapine-N-oxide (CNO) leads to activation of DREADD expressing neurons.



Project: Context-induced relapse to alcohol-seeking after voluntary abstinence

Substance abuse is a major health care problem. Accordingly, there is a real need to increase our fundamental understanding of the processes behind addiction, so that more targeted therapeutic strategies can follow. We have identified a potentially critical neural mechanism by which alcohol associated environments promote alcohol seeking during abstinence. We will further unravel the brain mechanisms of relapse to alcohol seeking, and will identify novel brain areas and circuits that future clinical studies can target in treatment-seeking alcoholics A limitation identified in animal models is that abstinence is achieved 'non-voluntarily' (experimenter-imposed). In humans, however, abstinence is typically voluntary (self-imposed), despite drug availability and often out of a desire to avoid the negative consequence associated with excessive alcohol use. A recently developed animal model addresses this limitation. In this model, the laboratory animal abstains voluntarily from alcohol use when alcohol-seeking is associated with a negative consequence. We will combine this novel animal model of relapse with an innovative procedure to manipulate neurons in defined neural circuits to determine which neuropeptides are critical for context-induced relapse to alcohol seeking.

Project Supervisor
Dr Erin Campbell

Project co-supervisor
Professor Andrew Lawrence

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: A circuit driving maternal behaviour / social reward

Women of childbearing age are at high risk for major depression, with the risk of depressive episodes increasing during pregnancy and new motherhood. Maternal depression can result in an altered interactional style with children: postnatally depressed mothers are less sensitive than non-depressed mothers when interacting with their offspring. This lack of maternal warmth and responsivity alongside hostile or rejecting mothering styles significantly increases the propensity of their children to develop psychopathologies later in life. Maternal neglect is associated with poorer cognitive outcomes as well as increased risk for developing depression, anxiety, and substance abuse in offspring. Despite the enduring effects of maternal neglect, little is known about its neurobiological underpinnings. A main reason for this is the lack of ethological models that adequately recapitulate the human experience. Indeed, most preclinical models have employed physical separation of mothers from their offspring. As such, a more ecologically valid preclinical model of maternal neglect is required. In this regard, we have compelling evidence for a specific brain pathway that is critical for adequate expression of maternal behaviour in mice. Inhibiting this pathway causes maternal neglect in mice in their natural (home cage) setting without the need for experimenter-enforced separation. We will use this preclinical model to identify the behavioural, circuit and neurochemical mechanisms of maternal behaviour using a multidisciplinary approach involving chemogenetics, pathway tracing, behaviour, gene & protein expression.

Project Supervisor
A/Prof Andrew Lawrence

- Ph.D
- Honours
- Master of Biomedical Science

Project: The oxytocin system in sugar and alcohol intake

Oxytocin is well-recognised for its role in labour, lactation and social interaction; however, it is also known to be involved in regulating fluid and salt intake. We have recently discovered a population of neurons that express the receptor for oxytocin and are located in the parabrachial nucleus of the hindbrain, which robustly suppress water and saline (NaCl) intake, but not food intake. We are now interested in investigating whether these neurons may also play a role in suppressing sugar, alcohol and non-caloric saccharin intake, which may suggest a role in addictive-like behaviours.

We will use genetically-modified mice that allow us to selectively manipulate this neuronal population by techniques such as optogenetics and DREADDs (designer receptors exclusively activated by designer drugs). We are also interested in directly observing these neurons using calcium imaging techniques, which allow us to visualise activity in the neurons in real-time while the mice are actively drinking. The project will also involve anatomical and electrophysiological studies to map out the neural circuitry of fluid intake.

Project supervisor
Dr Phil Ryan

Project co-supervisor
Prof Andrew Lawrence

- M.Phil/Ph.D.
- Master of Biomedical Science

Project: Investigating Alcohol-Related Dementia

Alcohol-related dementia (ARD) is one of the leading causes of secondary (preventable) dementia, and younger onset dementia (onset of symptoms prior to 65 years) in Australia. Together with the high rates of alcohol consumption in Australia, this means that ARD is becoming an increasingly urgent public health issue. The only treatment currently available for ARD is alcohol rehabilitation and abstinence. However, emerging evidence from animal models indicates that exercise may act as a protective factor against the neurotoxic effects of alcohol, and is even able to reverse some of the brain injury that occurs following alcohol exposure.

The aim of this project is to use a validated rodent model to:

1. Characterise the cognitive and neuropathological symptoms of ARD.
2. Evaluate the restorative effects of abstinence combined with voluntary exercise on these symptoms.

Project Supervisor
Dr Christina Perry

Project co-supervisor
Prof Andrew Lawrence

Project availability
- M.Phil/Ph.D.
- Master of Biomedical Science
- Honours

MAZZONE GROUP

Contact: **Prof Stuart Mazzone**

Email: **stuart.mazzone@unimelb.edu.au**

Location: **Department of Anatomy & Neuroscience**

The Respiratory Sensory Neuroscience Laboratory is interested in the sensory neuron populations that innervate the airways and lungs and the brain circuits that process respiratory sensory information. We use transcriptomic profiling to better describe the molecular characteristics of respiratory sensory neurons, viral tract tracing and modern molecular physiology to understand the organisation of function circuits in the brain and human functional brain imaging to assess plasticity in the central nervous system in patients with disease.

Project: Neuroinflammatory mechanisms in influenza viral infections

Influenza is a major cause of pulmonary disease. We have discovered bidirectional interactions between the nervous and immune systems that are important for determining the severity of influenza infections. This project will use surgical and molecular approaches in mice to further investigate the neural contributions to pulmonary inflammation during influenza. Techniques include small animal surgeries, chemogenetics, qPCR, immunohistochemistry, flow cytometry, microscopy.

Project supervisor
Dr Alice McGovern

Project co-supervisor
Prof Stuart Mazzone

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

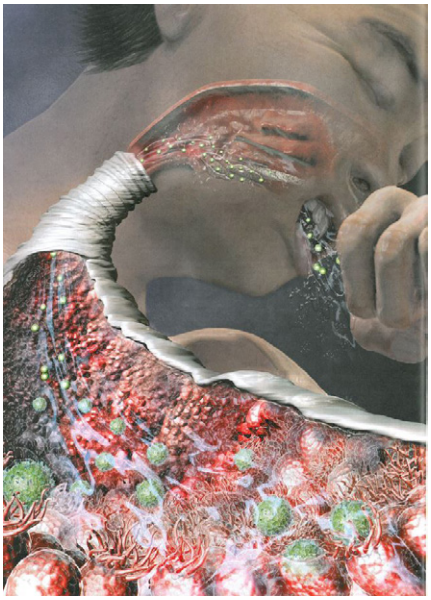
Project: Investigating brain networks processing respiratory sensations

Respiratory sensory neurons are critical for the ongoing physiological control of breathing as well as protecting against potentially damaging stimuli that could adversely affect ventilation. They do so by providing inputs to complex brain networks responsible for generating respiratory sensations and resultant behaviours. Changes in the excitability of these brain networks may be important for the development of coughing, dyspnoea and hyperreactivity characteristic of many lung diseases. In this project we are mapping the neural connections of airway sensory circuits in the central nervous system and employing molecular physiological approaches using optogenetics and chemogenetics to better define how respiratory sensations are encoded in the brain. Techniques include viral vector production, small animal surgeries, molecular physiology studies, microscopy.

Project supervisor
Prof Stuart Mazzone

Project co-supervisor
Dr Alice McGovern
Dr Aung Aung Kywe Moe

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science



MCCOLL GROUP

Contact: **Gawain McColl**

Email: **gmccoll@unimelb.edu.au**

Location: **Kenneth Myer Building**

Weblink: **https://www.florey.edu.au/science-research/scientist-directory/dr-gawain-mccoll**

The McColl group is explores brain ageing and the impact it has on neurodegenerative diseases. We use the nematode, *Caenorhabditis elegans*, to model the biology of ageing and late-life neurobiology. By reducing complexity and time scale, the study of simple organisms can provided a wealth of information about the biochemical systems and fundamental biological processes. Despite the relative simplicity of these animals the conservation of genetic and disease pathways between these nematodes and higher eukaryotes make it an effective in vivo model for study ageing and disease mechanisms.

Project: Ageing, Iron and Neurodegeneration

Age is the single biggest risk factor for major neurodegenerative diseases, such as Alzheimer's and Parkinson's disease. How ageing drives disease susceptibility is a fundamental but poorly understood question. To solve the mystery of brain ageing we propose to first understand it in a simpler animal. Our laboratory takes a fresh approach, using the nematode *Caenorhabditis elegans*, with its well-developed genetics, to explore the biological roles of iron. Metal ions, including those of iron, are essential for life with approximately half of all proteins using a metal ion co-factor. However, excess metal ions can be highly toxic. Organs such as the brain accumulates iron through life, which may contribute to disease risk. This project will explore why the handling of redox-active iron fatigues with age, and creates a toxic, pro-ageing biochemistry and drives cell death. In addition, this project will 1. Characterise the cellular consequences of age-dependent iron changes; and 2) Investigate cell type specific restoration of iron homeostasis to identify where iron toxicity occurs and if and how it spreads.

Project supervisor
Dr Gawain McColl

Project co-supervisor
Prof. Ashley Bush
M.Phil/Ph.D

- Honours
- Master of Biomedical Science

Project: Rapid Animal Models of Parkinson's disease

Parkinson's disease is a debilitating disorder, classically characterised by progressive and selective loss of dopaminergic neurons within the Substantia Nigra. By the time a patient presents with motor symptoms 60-70% of the nigral dopaminergic neurons have already been destroyed. Although current pharmacotherapies offer some effectiveness in early stages of disease, these medications offer only symptomatic relief and fail to protect the remaining neurons from eventual degeneration. Devising therapeutics that address not only the symptoms of Parkinson's disease but also the cause (so called 'disease modifiers') are of vital importance. While mammalian-based Parkinson's disease research is clearly a necessary step, sole reliance on mammalian models limits the rate at which new therapeutics can be identified. More rapid whole animal screening technologies are needed to develop therapeutics. We have identified the nematode *Caenorhabditis elegans* as being highly suited for studying neurodegeneration, genetic interactions and drug mode-of-action. The project will explore neuro-restorative compounds in rapid *Caenorhabditis elegans* models of dopaminergic cell loss, by 1) Characterising newly identified cell death inhibitors in novel animal models of dopaminergic cell loss; and 2) Investigating cell signaling pathways for effects on dopaminergic cell loss and subsequent neuroprotection by compounds.

Project supervisor
Dr Gawain McColl

Project co-supervisor
Prof. Ashley Bush

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

NITHIANANTHARAJAH GROUP

Contact: **Associate Professor Jess Nithianantharajah**

Email: **jess.n@florey.edu.au**

Location: **Florey Institute of Neuroscience and Mental Health**

Weblink: **https://www.florey.edu.au/science-research/scientist-directory/dr-jess-nithianantharajah**

The Synapse Biology & Cognition Laboratory is focused on understanding the role of synaptic genes in regulating the coordinated wiring and connectivity of the brain to support complex cognition and higher order processing. Sensory information from the environment is ultimately processed at the level of synapses, the connection between neurons that form the most fundamental information-processing units in the nervous system. Vertebrate synapses contain a large yet intricately organised signalling complex of proteins encompassing neurotransmitter receptors, scaffold proteins and cell adhesion proteins. Mutations in synapse genes can disrupt circuit formation and plasticity, leading to maladaptive behaviours that underlie mental disorder

Bridging the gap between preclinical and clinical cognitive testing, the touchscreen methodology that A/Prof Nithianantharajah was involved in developing at the University of Cambridge, provides an innovative tool for dissecting higher cognitive functions in rodents that is highly analogous to cognitive assessment of clinical populations. In our laboratory, we use genetically modified mice as models to study how genes important for regulating synapse function and plasticity selectively modulate cognitive behaviour. Our approaches combine in-depth behavioural analysis with advanced in vivo molecular, cellular and imaging techniques.

Project: Imaging excitatory-inhibitory imbalance on neural networks responsible for reward-based learning

This project will involve in vivo calcium imaging of neural activity in behaving mice during reward-based learning in touchscreen tasks.

Project: Understanding the neural basis of decision-making under uncertainty

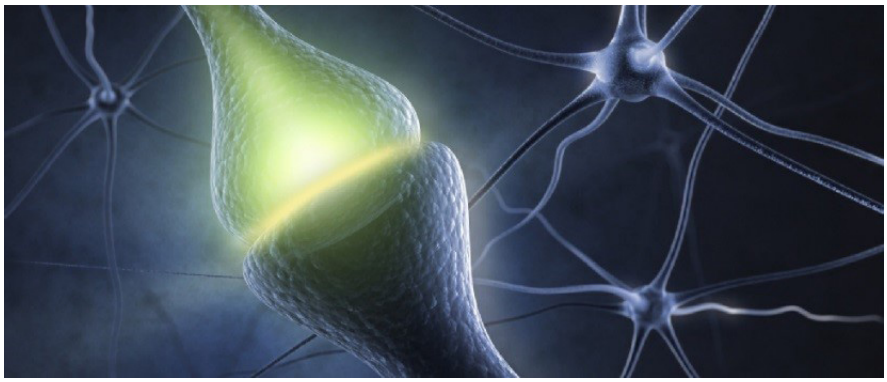
This project will use in vivo manipulations (optogenetics, calcium imaging) to elucidate processes underlying performance in a novel non-instrumental information seeking touchscreen task.

Project: Molecular and biochemical analysis of novel disease variants on synaptic protein stability in neurodevelopmental disorders

This project will involve advanced protein binding and stability assays to measure the functional impact of novel synapse gene mutations identified in neurodevelopmental disorders including Autism Spectrum Disorder, Intellectual Disability, and schizophrenia.

Project supervisor
Associate Professor Jess Nithianantharajah

- Ph.D.
- Honours
- Master of Biomedical Science



PALMER GROUP

Contact: **Assoc. Prof Lucy Palmer**

Email: **lucy.palmer@florey.edu.au**

Location: F**lorey Institute, Kenneth Myer Building**

The Neural Networks group uses various techniques to record from neurons *in vivo* including two photon calcium imaging, somatic and dendritic patch-clamp electrophysiology and optogenetics. Through this work, we investigate how sensory information is received, transformed and modulated in neurons, but also how this processing of synaptic input contributes to the overall neural network activity underlying learning and behaviour.

Project: The modulation of sensory perception by the prefrontal cortex.

This project will combine multiple state-of-the-art techniques including two-photon microscopy, patch-clamp electrophysiology and optogenetics (light to control neurons) *in vivo* to probe the influence of the prefrontal cortex on sensory perception. Specifically, the influence of prefrontal cortex communication on the activity of pyramidal neurons within the somatosensory cortex will be investigated during non-noxious sensory stimulation. The distal dendrites of cortical pyramidal neurons generate large NMDA-dependent voltage events, termed NMDA spikes, in response to sensory stimulation. The generation of these NMDA spikes are extremely important in neuronal response to sensory input and therefore whether prefrontal cortical activity modulates their generation and leads to changes in sensory perception will be investigated. The results of this study will reveal the cellular mechanisms underlying prefrontal cortex control of other brain regions and will therefore shed light on diseases involving prefrontal cortical dysfunction.

Project supervisor
AProf Lucy Palmer
Project co supervisor
Dr Marius Rosier

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: The neural basis of learning

Our memories define who we are. Whether it's a memory from our childhood or a memory from eating breakfast in the morning, all memories combine to contribute to how we react to everyday life. It is crucial that memories are formed and can be recalled at will. How the brain does this is largely mysterious. The brain consists of billions of individual neurons that are connected to one another forming a complex wiring pattern. An individual neuron receives thousands, sometimes tens of thousands, of inputs from other brain cells. Almost all of these inputs land onto a neuron's complex, tree-like branches, called dendrites. Dendrites then combine these thousands of inputs into action potentials, which is transferred to thousands of other neurons (and the process continues). This is how the brain communicates and changes to this cascade of events is how we make sense of our environment and learn new things.

Despite its importance in everyday life, little is known about the activity of neurons during learning and memory formation. Furthermore, even less is known about how dendrites alter their activity as we learn a new task. Since dendrites are the site of information transfer between neurons, their activity must reflect learning and memory formation. This project will use electrophysiology and two-photon calcium imaging to measure neural activity during learning and memory formation. Optogenetic manipulations will also be used to investigate the importance of dendritic integration in the animal's ability to successfully perform the learnt behaviour.

The results of this study are extremely important in understanding how neural and dendritic integration influences learning in the cortex, leading to a greater knowledge about the cortical activity underlying the processing of sensory information. Identifying the cellular mechanisms of the feedback functional connectivity is crucial not only for understanding higher brain functions but it also reveals potential targets for direct therapeutic intervention in the diseased brain where memory formation and learning is impaired such as dementia, traumatic brain injury and autism spectrum disorders (just to name a few).

Project supervisor
AProf Lucy Palmer

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: Measuring whole brain activity during behaviour

Understanding how the brain forms memories is currently one of the most important questions in neuroscience. Memory formation is a critical aspect of survival – we must learn and remember all aspects of our life, from facial recognition, to food location/ source. However, how the brain encodes memories is largely unknown and the focus of this project.

Here, memory formation and cortical activity during learning and decision making will be addressed using a widefield microscope which enables the surface of the entire mouse cortex to be measured. Here, using transgenetic mice with genetic calcium indicators, neural activity from multiple brain regions will be measured and compared while a mouse is learning a decision-based task. Involved brain regions will be perturbed using optogenetics, and the effect on the learned behaviour will be measured.

The results from this study will measure dendritic and neural properties of neurons which experienced increased activity during the formation of a memory.

Project supervisor
AProf Lucy Palmer

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

PANG GROUP

Contact: **Dr. Terence Pang**

Email: **terence.pang@florey.edu.au**

Location: **Florey Institute of Neuroscience and Mental Health**

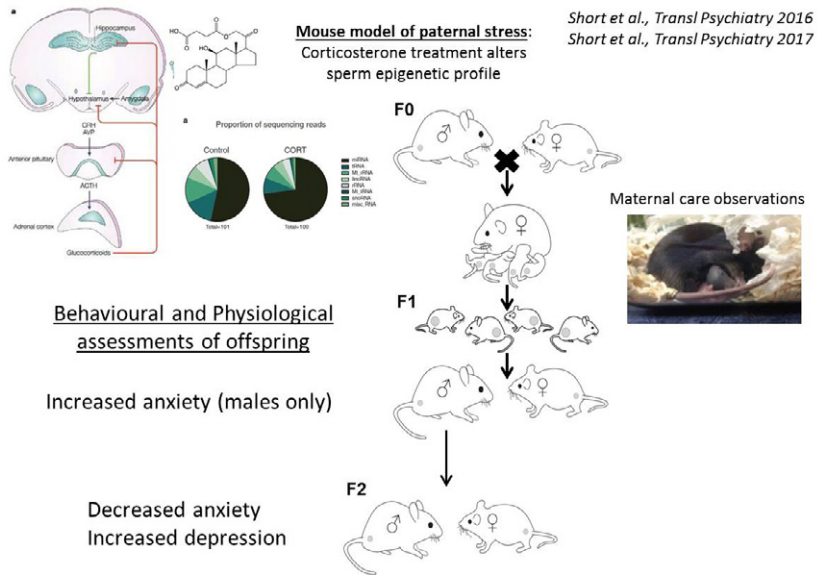
Weblinks: **https://www.florey.edu.au/science-research/scientist-directory/dr-terence-pang**

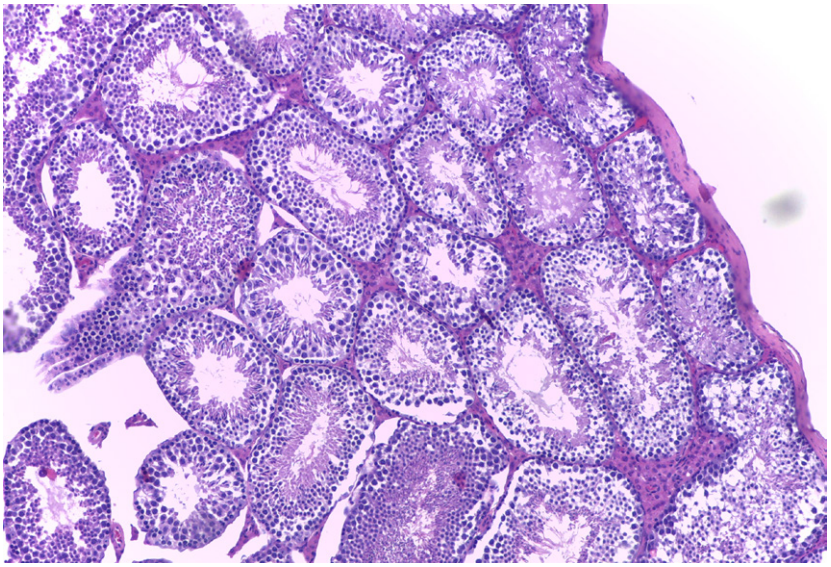
https://scholar.google.com.au/citations?user=jH30a9sAAAAJ&hl=en

My group is interested in the pathogenesis of psychiatric disorders, particularly stress-linked conditions such as anxiety disorder and major depression. We discovered that exposure of the paternal generation to stress can yield transgenerational effects on offspring behaviour and physical health. Our research takes a multidisciplinary approach by combining rodent behavioural studies, gene expression profiling of brain tissue, blood hormone assays, and screening of male reproductive health parameters.

Project: Transgenerational effects of paternal stress on offspring behaviour and cognition.

Paternal transgenerational inheritance is a fast-growing area of research with implications for how we may address mental and physical health issues of future generations. Our lab discovered that prolonged exposure of the male germ line to low-level stress alters the sperm epigenome and is associated with the emergence of anxiety and depression-related behaviours in offspring and grand-offspring. Subsequent studies have uncovered differential expression of neurotrophic and stress-response genes in the hippocampus and prefrontal cortex, providing the rationale to investigate if cognitive function of the progeny is compromised. We are also broadening our study of offspring behaviour by examining how the animals behave under stressful situations. Students will engage in studies of a unique mouse model of paternal stress and be trained in rodent behavioural testing, anatomical dissections and histological studies, systematic assessment of the hypothalamus-pituitary-adrenal axis integrity, and gene expression profiling. There is also scope for additional research of beneficial stress-modifying lifestyle factors and pharmacotherapies to moderate the transgenerational effects of ancestral stress exposure.





Project supervisor
Dr Terence Pang

Project co-supervisor
Prof Anthony Hannan

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

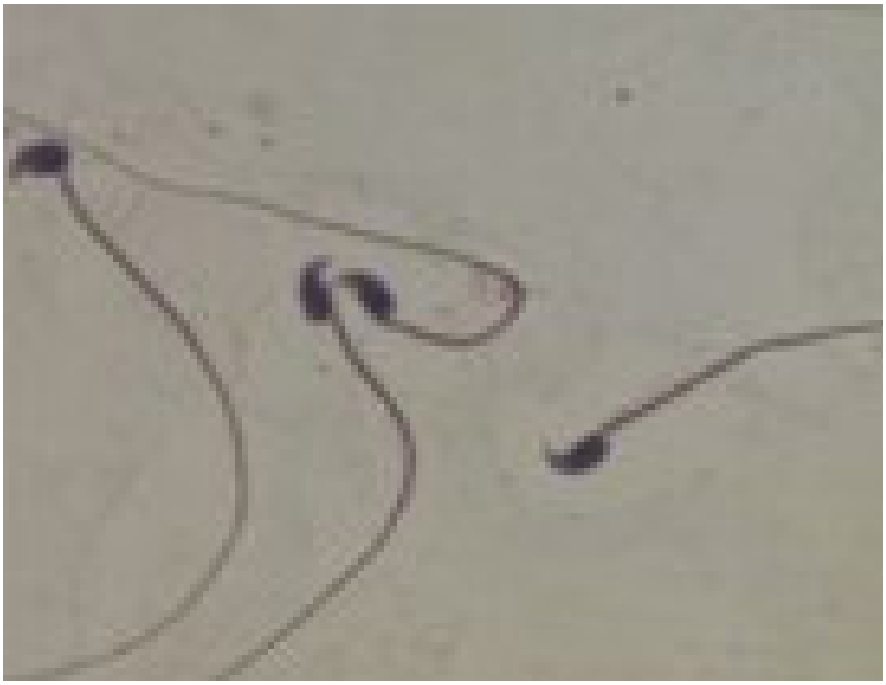
Project: How do paternal experiences impact offspring behaviour, physiology and reproductive fitness?

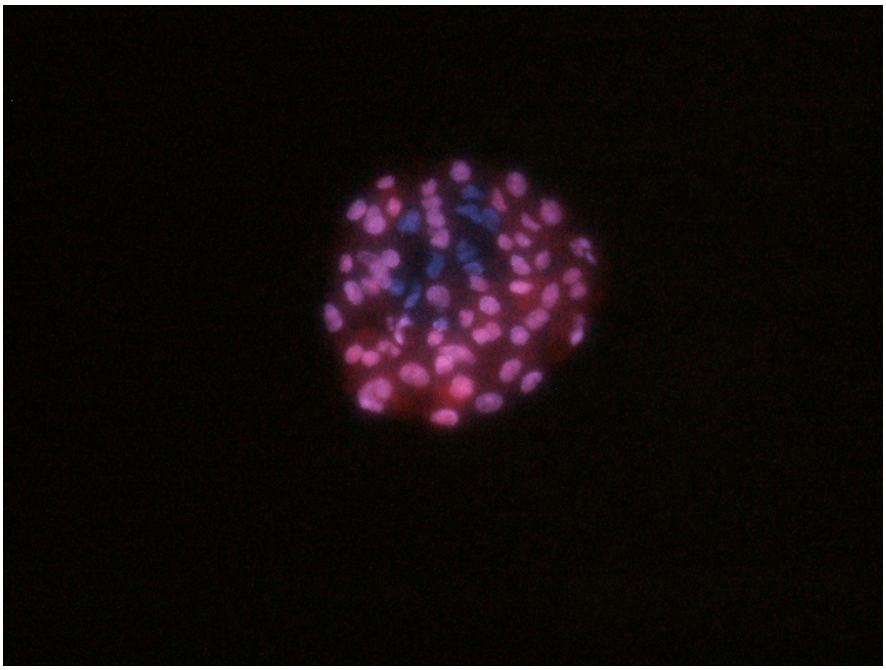
The negative impacts of trauma on the mental health and physical well-being of individuals are well-described. Surprisingly, little is understood of how stress regulates male reproductive health. Recent epidemiological studies have reported learning deficits and mood-related behavioural problems in children born to parents with a history of war-related trauma. The biological mechanisms underlying this intergenerational effect of parental trauma is unknown. This cross-disciplinary project aims to discover how traumatic stress affects male reproductive health, focussing on early life trauma exposure. Using rodent models of traumatic stress of varying chronicity, students will have the opportunity to investigate how offspring behavioural phenotypes are influenced by paternal history of trauma. That is linked to studies of sperm health and male fertility, as well as early embryonic development. Students will be trained in rodent behavioural testing, performing anatomical dissections, and RNA/DNA isolation techniques for gene expression profiling studies. There is also opportunity to engaged in morphological and histological studies of embryos and reproductive organs. This project is ideal for an individual looking for a diverse research experience in behavioural neuroscience and reproductive biology.

Project supervisor
Dr Terence Pang

Project co-supervisor
Prof David Gardner (School of Biosciences)

- M.Phil/Ph.D.
- Honours- 1
- Master of Biomedical Science





STAMP & HAO GROUP

Contact: **Lincon Stamp and Marlene Hao**

Email: **lstamp@unimelb.edu.au; hao.m@unimelb.edu.au**

Location: **Department of Anatomy & Neuroscience**

Weblinks: **https://biomedicalsciences.unimelb.edu.au/sbs-research-groups/department-of-anatomy-and-neuroscience/development-of-the-enteric-nervous-system**

Our group is interested in the development of the enteric nervous system and stem cell therapies for enteric neuropathies. The enteric nervous system is responsible for the co-ordinated control of gut function. Enteric neurons and glia are located in a network of interconnecting ganglia within the wall of the gastrointestinal tract. Correct development of this nervous system is crucial for proper control of digestive function. Please refer to our website for more information on our research and publications:

Project: Stem cell therapy to treat Hirschsprung's disease

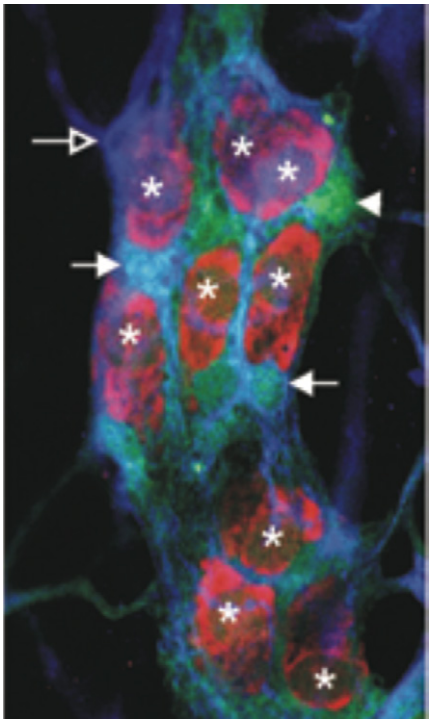
Hirschsprung's Disease arises from the failure of neural crest cells to migrate to the anal end of the colon, resulting in a lack of enteric neurons in the unpopulated region. As the enteric nervous system is crucial for gastrointestinal function, there is no propulsive activity in the aganglionic region and there is a build-up of gut contents, which can prove fatal if left untreated. Hirschsprung patients currently undergo "pull-through" surgery to remove the aganglionic region of bowel. Whilst this is life-saving, most patients suffer chronic, long-term complications, including constipation, faecal soiling, and associated psychosocial problems.

Stem cell therapy, where missing enteric neurons are replaced, is an exciting area of research. In this project, we are using a rat model of Hirschsprung Disease to investigate the clinical application of cell therapy for Hirschsprung patients.

Project supervisor
Dr. Lincon Stamp

Project co-supervisor
Dr.Marlene Hao, A/Prof Sebastian King

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science



Stem cells (green) transplanted into the colon of mice differentiate into enteric neurons (red) and glia (blue).

Project: Understanding interactions between gut epithelial stem cells and enteric neurons

This project aims to investigate the interaction between gut neurons and the epithelial stem cell compartment, as well as the relationship between age-related loss of enteric neurons and changes in gut epithelial stem cells. The role of epithelial stem cell-nerve communication, and the signalling pathways mediating it, are currently poorly understood.

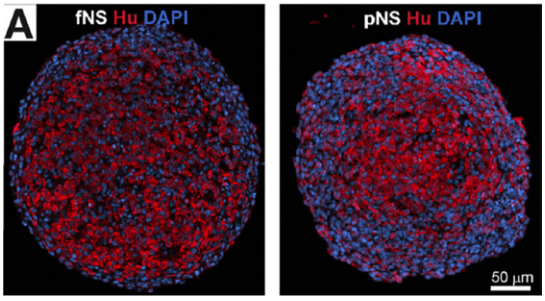
This study, which includes novel co-culturing of organoids and enteric neurospheres, will identify signalling pathways and cellular mechanisms by which nerves influence the epithelia during homeostasis and ageing.

The outcome of the project will be a better understanding of the biology of the body's most highly proliferative, long-lived stem cells; intestinal epithelial stem cells.

Project supervisor
Dr. Lincon Stamp

Project co-supervisor
Dr. Marlene Hao

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science



Neurospheres from foetal and postnatal cells contain Hu-expressing neurons (red). All cell nuclei are stained by dapi (blue).

Project: Circadian plasticity of the enteric nervous system

Correct control of gut motility is crucial for the health and function of all animals. Gut function changes throughout the 24-hr day/night cycle with increased motility when we are awake. What controls these daily oscillating changes in gut output is unknown. Our data show there are daily alterations in the enteric nervous system, which is located in the gastrointestinal tract and controls its function. In this project, we will examine how plasticity of the enteric nervous system through the circadian cycle leads to changes in gut function.

Project supervisor
Dr. Marlene Hao

Project co-supervisor
Dr. Lincon Stamp
Project availability

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: A gut feeling about new therapies for glioma

Gliomas are a very aggressive form of brain cancer, with a very poor 5-year survival rate. Gliomas can arise from over-proliferation of glial cells or stem cells in the brain. Glial cells are a prominent part of the enteric nervous system in the gut.

In this project, we will use a novel line of transgenic mice to investigate gene expression patterns between glial cells in the brain and the gut using RNA-sequencing technology and bioinformatic analysis.

Project supervisor
Marlene Hao

Project co-supervisor
Lincon Stamp

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

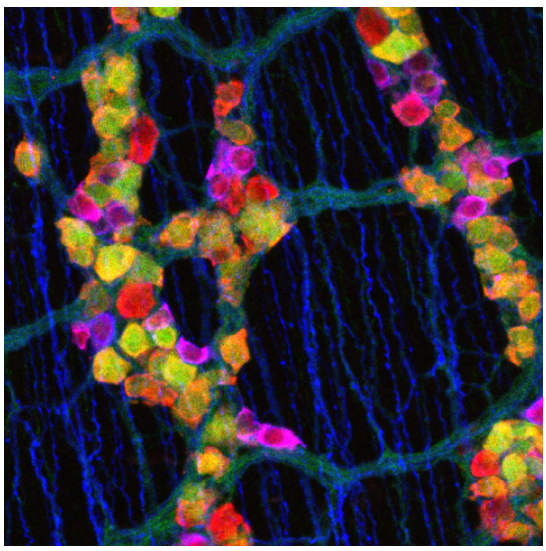
Project: Glutamate in the enteric nervous system

Glutamate is a major excitatory neurotransmitter in the central nervous system (CNS). Unlike the CNS, the major excitatory neurotransmitter in the enteric nervous system is acetyl-choline. Although it has been detected in the gut, the role of glutamate in enteric neural function has not been well elucidated. In this study, you will use immunohistochemistry and calcium imaging to investigate the role of mGluR1 receptors in the ENS.

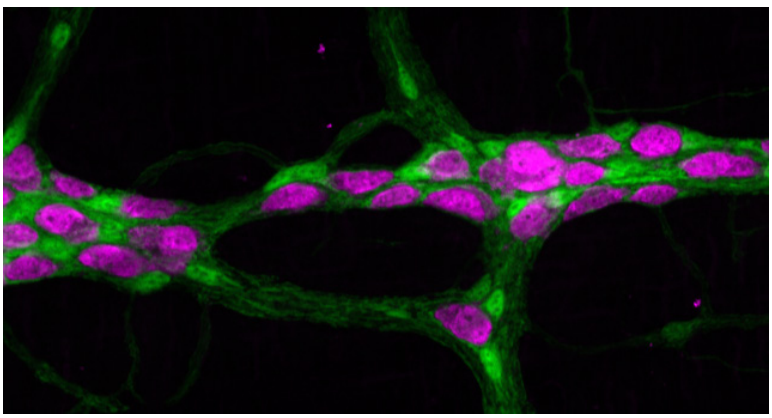
Project supervisor
Marlene Hao

Project co-supervisor
Joel Bornstein

- Honours
- Master of Biomedical Science



Different subtypes of neurons in the enteric nervous system. Excitatory cholinergic neurons (green) and inhibitory nitregic neurons (blue) are co-localised with a pan-neuronal marker.



Glial cells in the enteric nervous system (green) surround neuronal cell bodies (magenta).

THOMPSON GROUP

Contact: **Dr. Lachlan Thompson**
Email: **lachlant@unimelb.edu.au**
Location: **Florey Institute of Neuroscience and Mental Health**

Our laboratory is interested in the idea that stem cells can repair the damaged brain. There are two broad strategies we are pursuing. The first is neural transplantation. It is an approach that has had some success clinically for Parkinson's disease and involves the transplantation of new neurons directly into the patient's brain in order to functionally compensate for those lost to the disease. We are continuing to explore and optimise this as a therapeutic option not only for Parkinson's disease but also for other neurological conditions such as stroke and motor neuron disease. The second strategy is based on the idea that the brain retains some capacity for 'self-repair' through neurogenesis. Part of our research program seeks to characterise the brain's own capacity to generate new neurons in response to injury and to manipulate this response in favour of therapeutic outcomes

Project: Parkinson's disease in a dish

Pluripotent stem cells can be used to generate a wide variety of neuronal subtypes relevant for repair of the central nervous system. Recently we showed that cortical neurons can be transplanted into the part of the cortex damaged by a focal stroke and have a remarkable capacity to integrate into the existing host circuitry in order to restore motor function. This project will extend on these findings to explore whether we can restore multiple circuits in more severe models of stoke affecting multiple brain region by transplanting multiple neuronal cell types. The project will utilise a number of in vitro and in vivo techniques including: human pluripotent cell culture; immunochemistry; stereotaxic surgery; analysis of animal behaviour; histology and microscopy

Project Supervisor
Dr Lachlan Thompson

Project Co-supervisor
Dr Jennifer Hollands

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: Rebuilding the brain after stroke

Pluripotent stem cells can be used to generate a wide variety of neuronal subtypes relevant for repair of the central nervous system. Recently we showed that cortical neurons can be transplanted into the part of the cortex damaged by a focal stroke and have a remarkable capacity to integrate into the existing host circuitry in order to restore motor function. This project will extend on these findings in order to explore whether we can restore multiple circuits in more severe models of stoke affecting multiple brain region by transplanting multiple neuronal cell types. The project will utilise a number of in vitro and in vivo techniques including: human pluripotent cell culture; immunochemistry; stereotaxic surgery; analysis of animal behaviour; histology and microscopy.

Project Supervisor
Dr Lachlan Thompson

Project Co-supervisor
Dr Jennifer Hollands

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: Development of Stem Cell based therapies for Motor Neuron Disease.

Recent advances in stem cell biology allow for the on-demand generation of spinal motor neurons from human pluripotent stem cells. Our laboratory has been exploring the possibility that these neurons can be implanted directly into the spinal cord in order to functionally compensate for those lost to the disease process. This project will seek to understand the capacity for implanted motor neurons to appropriately integrate into host circuitry, including innervation of peripheral targets. We will also explore the concept that the implanted neurons can protect the host neurons from the disease process.

Project supervisor
Dr Lachlan Thompson

Project co-supervisor
Dr Stefano Frausins

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

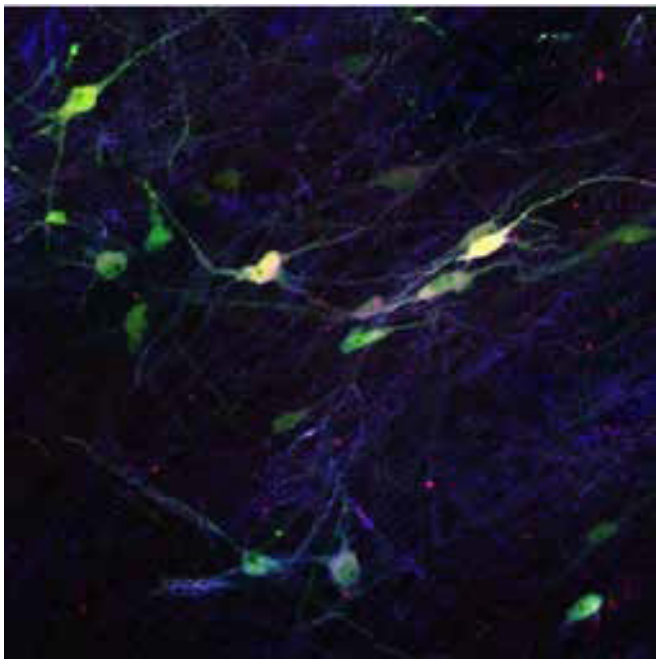


Figure: Functional midbrain dopamine neurons generated from human pluripotent stem cells

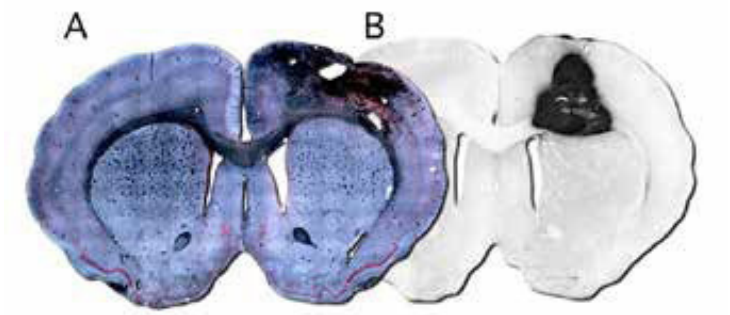


Figure. A) Damage to the cortex caused by focal ischemia. B) A stem cell derived graft of new cortical neurons to replace those lost to the ischemic damage.

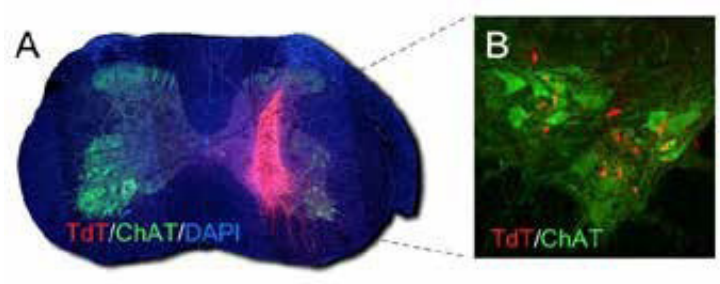


Figure. A) Graft of human stem cell derived neurons engineered to express a fluorescent protein (TdT) to allow for identification in the host brain. B) The transplanted neurons migrate to and intermingle with the diseased host motor neurons (ChAT) and may provide trophic support

TURNER GROUP

Contact: **Assoc. Prof Bradley Turner**

Email: **bradley.turner@florey.edu.au**

Location: **Florey Institute of Neuroscience and Mental Health**

The Turner lab is interested in modelling neurodegenerative diseases affecting the motor system using patient stem cell and animal models, spanning pediatric and adult motor neuron diseases.

Project: Investigating the autophagy pathway in a novel C9ORF72 mouse model of motor neuron disease

Motor neuron disease (MND) is a neurodegenerative disease characterised by cytoplasmic accumulation and aggregation of proteins which are implicated in motor neuron death. Strategies that improve proteostasis and clear these misfolded proteins in motor neurons are therefore an attractive therapeutic approach for MND.

Our group is interested in autophagy, the main catabolic pathway in neurons that targets and degrades misfolded proteins, aggregates and damaged organelles. C9ORF72 mutation is the largest genetic cause of MND affecting 40% of familial MND cases and 8-10 % of sporadic ALS. This project will investigate the autophagy pathway in a novel C9ORF72 mouse model and will employ advanced microscopy, immunohistological and image analysis techniques.

Project supervisor
A/Prof Bradley Turner

Project Co-supervisor:
Dr. Nirma Perera

- M.Phil/Ph.D.
- Honours

WELLS GROUP

Contact: **Prof. Christine Wells**

Email: **wells.c@unimelb.edu.au**

Location: **Kenneth Myer Building**

Weblink: **www.stemformatics.org/atlas/imac**

The Wells laboratory uses pluripotent stem cells to study tissue-resident immune cells such as macrophages and microglia to model specific disease or activation states in the laboratory dish.

We host the www.stemformatics.org resource and use this to understand the genetic networks underpinning cell differentiation and molecular identity. We are particularly interested in discovering and characterising new molecular controllers of immune cell function during tissue inflammation or injury – one example is the role of the C-type lectin Mincle on resident tissue macrophages in exacerbating neuroinflammation in brain and eye after injury.

Project: The iMAC atlas and the designer macrophage

The Wells laboratory has generated a comprehensive atlas of human resident tissue macrophages and benchmarked laboratory models against this compendium. Cells that have been generated in a laboratory contain unique culture-associated gene regulatory programs. The project has two parts – the first is to further develop the atlas by representing new activation or differentiation states, and validating these using new data types, such as single cell RNAseq and CITE-seq.

By mathematically modelling the genetic networks that are responsible for specific and desirable aspects of a cell, the second part of the project is to engineer these aspects in the laboratory, borrowing tools from cell reprogramming and genome editing technologies. This project is suitable for mathematics/computational students or biology students, and aspects can be undertaken as part of an honours or masters program. (https://www.stemformatics.org) and designer cell, please read the following papers from the laboratory).

Project supervisor
Professor Christine Wells

Project co-supervisor
Dr Jarny Choi

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

Project: Rescuing orphan proteins

Orphan proteins are genes with predicted open reading frames, but whose Location: and function has not been previously characterised. The Wells laboratory has identified a number of orphan proteins whose expression in macrophages indicate a role in innate immunity. Students will be assigned an orphan to characterise from first principles. The project has two parts – the first is to use the bioinformatics tools in the lab to assess which tissues and cells the orphan protein is expressed in. The second part of the project is to use CRISPR/CAS9 to tag the orphan in stem cells, so that it's movement in the cell can be visualised through microscopy methods. The student will gain experience in molecular biology methods and stem cell culture, including differentiation to different cell types. This project is suitable for biology or bioengineering students, and aspects can be undertaken as part of an honours or master's program.

Project Supervisor
Professor Christine Wells

- Honours
- Master of Biomedical Science

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For Mincle in sterile inflammation please see:

8 Thiruma Arumugam, Silvia Manzanero, Milena Furtado, Patrick Biggins, Yu-Hsuan Hsieh, Mathias Gelderblom, Kelli MacDonald, Ekaterina Salimova, Yu-I Li, Othmar Korn, Deborah Dewar, I Mhairi Macrae, Robert Ashman, Sung-Chun Tang, Nadia Rosenthal, Marc Ruitenberg, Tim Magnus, Christine Wells (2016) An atypical role for the myeloid receptor Mincle in CNS injury. Journal of Cerebral Blood Flow and Metabolism. 2017 Jun;37(6):2098-2111

9 Imai T, Matsumura T, Mayer-Lambertz S, Wells CA, Ishikawa E, Butcher SK, Barnett TC, Walker MJ, Imamura A, Ishida H, Ikebe T, Miyamoto T, Ato M, Ohga S, Lepenies B, van Sorge NM, Yamasaki S. (2018) Lipoteichoic acid anchor triggers Mincle to drive protective immunity against invasive group A Streptococcus infection. Proc Natl Acad Sci U S A. 2018 Nov 6;115(45):E10662-E10671. doi: 10.1073/pnas.1809100115.

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WILHELM GROUP

Contact: **Dr. Dagmar Wilhelm**

Email: **dagmar.wilhelm@unimelb.edu.au**

Location: **Department of Anatomy & Neuroscience.**

Weblink: **https://biomedicalsciences.unimelb.edu.au/sbs-research-groups/department-of-anatomy-and-neuroscience/development-of-the-enteric-nervous-system**

The ultimate goal of our research is to understand the genetics of sex determination and gonad development, and how failure results in human disorders of sex development and infertility. Disorders/differences of sex development (DSDs) refer to congenital conditions in which the development of chromosomal, gonadal or anatomical sex is atypical. They are very common, with an estimate of approximately 1 in 4,500 births. They have profound psychological and reproductive consequences for the patient, which are also often prone to testicular or ovarian cancer later in life. Surprisingly, although many genes have been identified which play a role in these processes for almost 70% of cases that we still do not know the underlying cause. Clearly, the identification of new genes and regulatory mechanisms involved in the formation of testis and ovary is critical for understanding the molecular pathology of DSDs.

Project: The role of the prorenin receptor in male and female infertility

The prorenin receptor is best known for its role in the renin-angiotensin system (RAS). However, recent research also shows that it plays multiple roles independent of pro/renin binding. We have shown that loss of the prorenin receptor in mouse somatic cells of the gonads results in male and female infertility. This project characterizes its role in fertility using mouse and Drosophila as model systems.

Project supervisor
Dr Dagmar Wilhelm

Project co-supervisor
Dr Dan Bird

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science

WILKINSON-BERKA GROUP

Contact: **Professor Jennifer Wilkinson-Berka**

Email: **Jennifer.wilkinsonberka@unimelb.edu.au**

Location: **Department of Anatomy & Neuroscience**

The Retinal Vascular Biology and Inflammation group is interested in understanding the factors that contribute to the development of major causes of vision loss and blindness across the globe; diabetic retinopathy in people of working age and retinopathy of prematurity in children. Our research focusses on various pathways that are involved including the immune system, oxidative stress, hypertension and advanced glycation end-products. We work with leading scientists and clinicians in order to translate our findings to human studies.

Projects: Modulating diet to treat retinopathy of prematurity and diabetic retinopathy

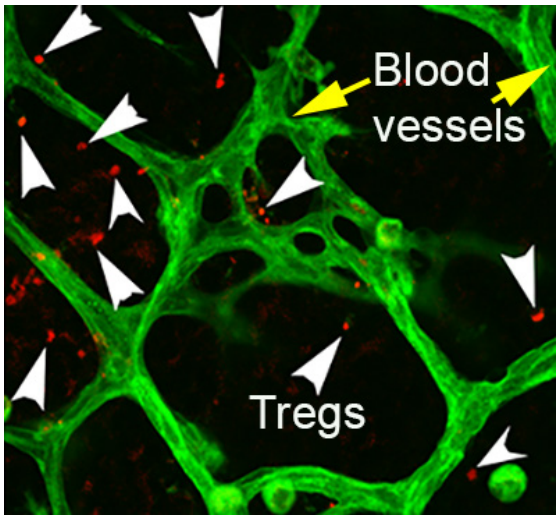
Retinopathy of prematurity (ROP) and diabetic retinopathy are diseases that damage the retinal microvasculature and can result in vision loss and blindness due to vascular leakage, vaso-obliteration and neovascularization. Unfortunately, there are no preventative treatments for ROP and diabetic retinopathy, with treatments administered to the eye when damage to the retina is established. ROP is a disease of the developing retinal vasculature that occurs in some babies who are born early and small. Diabetic retinopathy is the major cause of vision loss and blindness in people of working age. 382 million people around the globe have diabetes mellitus and this number is predicted to reach almost 600 million by 2030. Australia has not been spared: 250 people develop diabetes each day and 1.7 million are currently living with the disease. Moreover, indigenous Australians are 8 times more likely to develop diabetes and diabetic retinopathy.

The projects offered in the laboratory, arise from our recent publication in Nature Communications (see below) which described for the first time that regulatory T cells (Tregs) of the adaptive immune system penetrate into the retina in an animal model of ROP. We demonstrated that boosting the number of Tregs reduced vision-threatening vascular pathology and inflammation in the retina. Our data led us to evaluate if natural treatment approaches based on particular diets that alter the balance of anti-inflammatory Tregs and injurious immune cells, could reduce ROP, diabetic retinopathy and hypertensive diabetic retinopathy. In these projects, students will use experimental approaches including confocal microscopy, molecular biology and flow cytometry to determine if various diets and nutrients have a deleterious or beneficial effect on the retina in mice.

Deliyanti D et al. Foxp3+ Tregs are recruited to the retina to repair pathological angiogenesis. Nature Commun. 2017 Sep 29;8(1):748. doi: 10.1038/s41467-017-00751-w.

Project supervisor: Jennifer Wilkinson-Berka

- M.Phil/Ph.D.
- Honours
- Master of Biomedical Science



For more information:
Website: biomedicalsciences.unimelb.edu.au/departments/anatomy-and-neuroscience

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