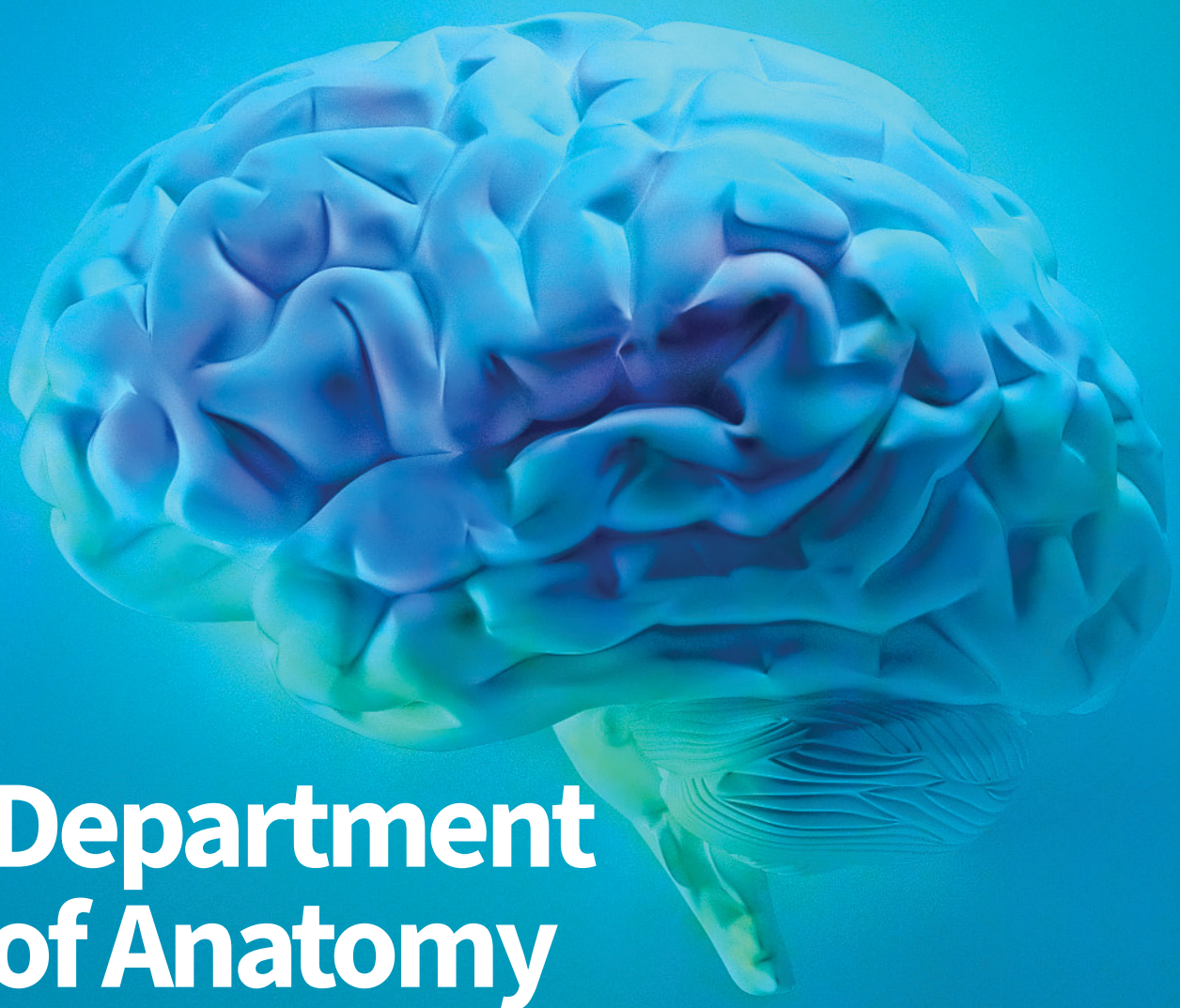
THE UNIVERSITY OF MELBOURNE



Department of Anatomy and Physiology 2024

Research Projects, Honours, Masters and PhD

Welcome

The decision to undertake an Honours year or a Masters degree is an important one that provides substance to your undergraduate degree. You get to see up close the workings of a research laboratory and gain the ability to put your scientific knowledge into practice.

It can be the first step towards an independent scientific career when you get the chance to pursue a research area of interest. This is likely to be the path for a small minority, but the skills learnt are valuable in many areas of life and in multiple careers. The extra qualification will also help set you apart from competitors when seeking employment or entry into other courses or specialties.

There are many things to consider – the research topic, your need and desire to undertake additional, advanced coursework, the laboratory and its resources, the potential supervisor and the departmental support of students.

The Department of Anatomy and Physiology has a strong record of award-winning research training and mentorship with our graduates securing leadership roles in universities, institutes, industry and in the private sector. We are very proud of our students and have developed a carefully structured program of coursework to complement your developing laboratory and analytical skills. The Department environment provides support in a number of ways for our Honours and Masters students, but perhaps none is more important than the friendship, advice and mentoring they receive from other graduate students.

This booklet provides information that will help you decide on a potential research project in Anatomy and Physiology at Honours and Masters Level and perhaps beyond to your PhD.

Our research is focused on themes related to metabolic and cardiovascular sciences, muscle biology, sensory and systems neuroscience, stem cells, and developmental biology and Learning and Teaching. Take your time and look at the different projects on offer. Identify projects that appeal to you and contact potential supervisors for more information and visit their laboratories. Ask lab heads, staff and students about the projects and your potential career options with the new qualification. Be assured, supervisors are very interested in talking to you and you should be confident in making that approach.

The Department of Anatomy and Physiology offers many exciting research opportunities and we welcome the chance to discuss these with you.

Professor Matthew Watt
Head of Department

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 75points of research and 25points of coursework, that commences mid-February and finish 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 contact with potential Honours supervisors.

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, 3 and mid year. 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.

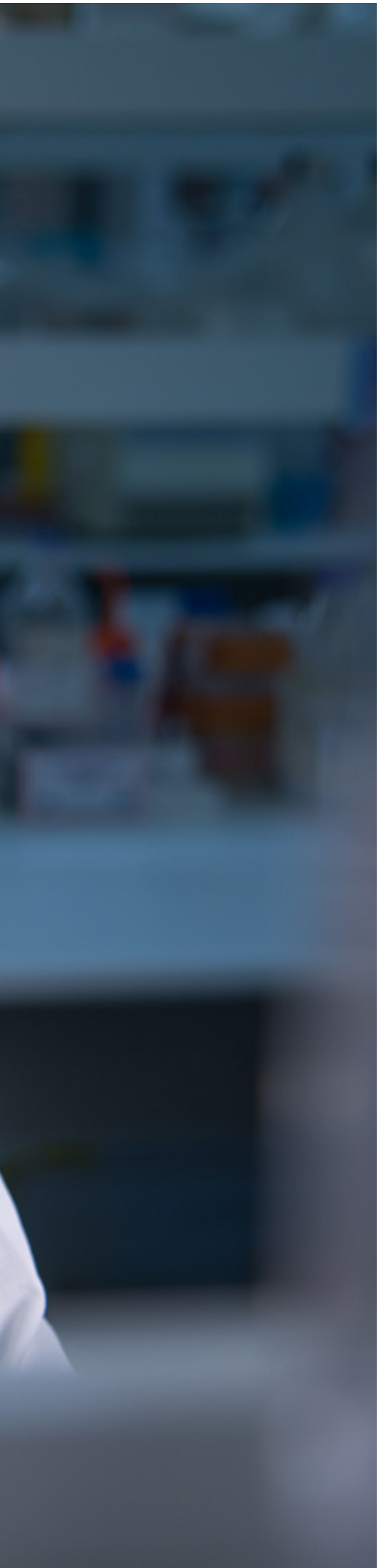
Selecting a Project

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:

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

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

https://biomedicalsciences.unimelb.edu.au/departments/anatomy-and-physiology

How to apply

- Review the list of prospective projects and supervisors in this handbook or online at https://biomedicalsciences.unimelb.edu.au/departments/anatomy-and-physiology
- Identify projects of interest and contact the project supervisor to explain your research interests and provide your curriculum vitae (CV) and academic transcripts.
- Once you have confirmed a project and supervisor apply online at https://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 a 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

Honours & Masters

If you a third-year student currently enrolled in Bachelor of Biomedical Science or Bachelor of Science and are considering enrolling to do Honours or Masters within the Department of Anatomy and Physiology in 2024 you can apply for a Summer Research Studentship or Vacation Scholarship to work on a supervised research project. The studentship provides a small living allowance to enable you to work on a laboratory-based project for a period of 4 or more weeks over the summer break. The purpose of the Summer Research Studentships and Vacation Scholarships is to provide an opportunity for undergraduates to gain first-hand experience in research.

Over the summer break, up to four Studentships and Vacation Scholarships may be available to the best qualified candidates.

You will need to discuss a project with a potential supervisor before applying. Most supervisors listed in this booklet will be happy to discuss summer projects with you.

For application forms and information, Please check out the following pages for further information:

mdhs.unimelb.edu.au/study/scholarships/n/vacation-scholarship

mdhs.unimelb.edu.au/study/scholarships/n/r.d.-wright-prize-and-scholarship

or Biomedical Science AcademicServices (biomedsci-academicservices@unimelb.edu.au) for further information

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

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Metabolic and Cardiovascular Sciences

Delbridge / Weeks Group

Contact: Prof Lea Delbridge
Email: lmd@unimelb.edu.au
Location: Department of Anatomy and Physiology

The Cardiac Phenomics Lab, along with the Cardiac Signalling Group, seeks to understand how the heart response to stress can be managed to minimize the damaging impacts of a variety of disease conditions. We investigate responses of the working 'pumping' heart, of specialized muscle tissues and cells from different regions of the heart, and of molecular signalling processes. As our name suggests, we look at how the cardiac 'genome' (the genetically defined heart) is translated in different stressor situations to create the 'phenome' (the structurally and functionally defined heart).

One of our focus areas is to explore the molecular signalling events involved in various heart failure types. Our pre-clinical work focuses on cardiac pathology arising from Type 1 and Type 2 diabetes and on the factors which determine how female and male hearts respond differently to stress and disease challenges. These areas of heart health are of critical significance in shaping the demographics of cardiovascular disease. We use experimental models to mimic human disease conditions, and we look for links between the performance of single muscle cells and the functioning heart.

Our goals are to inform the development of new treatments for diabetic cardiomyopathy and heart failure and to understand how for women and men, cardiac 'difference' may be managed with optimized therapeutic tools. Student projects could incorporate a range of methodologies including animal dietary and pharmacologic treatments, instrumented working heart preparations, immunohistochemistry, cell culture and adenoviral expression manipulation, cell kinetic imaging, biochemical assays, confocal microscopy, big data "omics" (e.g. transcriptomics, proteomics, phosphoproteomics), real-time PCR, and Western blot techniques.

Projects are particularly suitable for MSc students, as there is scope for progression to publication within the degree time frame and research work is supported by complementary skills development coursework. As part of the Cardiac Research Consortium (Australia and New Zealand), our projects involve multiple campus opportunities in Melbourne (LaTrobe University, Baker Heart & Diabetes Institute) and New Zealand (University of Auckland). There are also the prospects of Study-away opportunities with international collaborators (USA, Canada, Europe & UK).

Project: Understanding glycogen dysregulation in diabetic heart failure

Globally, diabetes is an epidemic disease with a specific cardiopathology independent of associated cardiovascular risk profiles. Diabetic hearts are more vulnerable to developing failure, especially after a myocardial infarct. Our work focuses on understanding the metabolic and structural changes leading to both diastolic and systolic dysfunction, examining how circulating glucose and insulin impacts on cardiopathology and identifying potential molecular targets for intervention. This project will utilise experimental models of type 1 and type 2 diabetes to

investigate the molecular and structural adaptations in the diabetic heart. We use cutting edge gene delivery and gene editing tools to create boutique experimental models of disease.

Project Supervisor:
Prof Lea Delbridge

Project Co-supervisor:
Dr Kimberley Mellor

Project Availability:
- PhD
- Master of Biomedical Science

Project: Is a ‘fat heart’ an especially vulnerable heart?

Maintaining normal rhythm properties is essential to heart function. Sustained arrhythmias (including atrial fibrillation) increase significantly with aging and in obesity. Often evident in otherwise ‘healthy’ asymptomatic patients, these sustained arrhythmias represent a primary component of cardiac demise. Understanding the cellular mechanisms driving arrhythmias is crucial to developing new effective therapies. Recent evidence has emerged indicating that accumulation of the fat around the heart (pericardial adipose) may be crucial to the development of sustained arrhythmias in the aged/obese population. Pericardial adipose levels are known to increase markedly in obesity, with aging, and in post-menopausal women – all important risk factors for cardiovascular disease. Our very recent data indicate that pericardial adipose may release proteins that exert a paracrine effect on the heart muscle to increase vulnerability to arrhythmias. This project will use molecular and tissue recording studies of human and rodent tissues to further understand how cardiac adipose contributes to the development of cardiac arrhythmias.

Project Supervisor:

Prof Lea Delbridge

Project Co-supervisor:

Dr James Bell

Project Availability:

- PhD
- Master of Biomedical Science

Project: Developing novel biomarkers for diabetic heart failure

Impaired diastolic relaxation is an early sign of diabetic cardiomyopathy and involves increased heart wall stiffness and abnormal filling during the diastolic period of the cardiac cycle. The early occurrence of diastolic dysfunction in otherwise ‘healthy’ asymptomatic diabetic patients has been extensively reported and is prognostic of later occurrence of heart failure and increased mortality. In the diabetic heart, irreversible modifications of certain cardiac proteins is correlated with impaired heart relaxation. Our data demonstrate that these protein modifications may contribute to impaired cardiac relaxation, indicating that small changes in protein structure can have large implications for diastolic function in diabetes. Specific characterisation of these key protein modifications offers the opportunity for biomarker development for use in the early detection of subclinical diabetic cardiomyopathy and monitoring of therapies. This project will involve work with experimental models of disease and clinical biopsy samples, as part of an associated project to develop biomarkers for early detection of cardiomyopathic disease.

Project Supervisor:

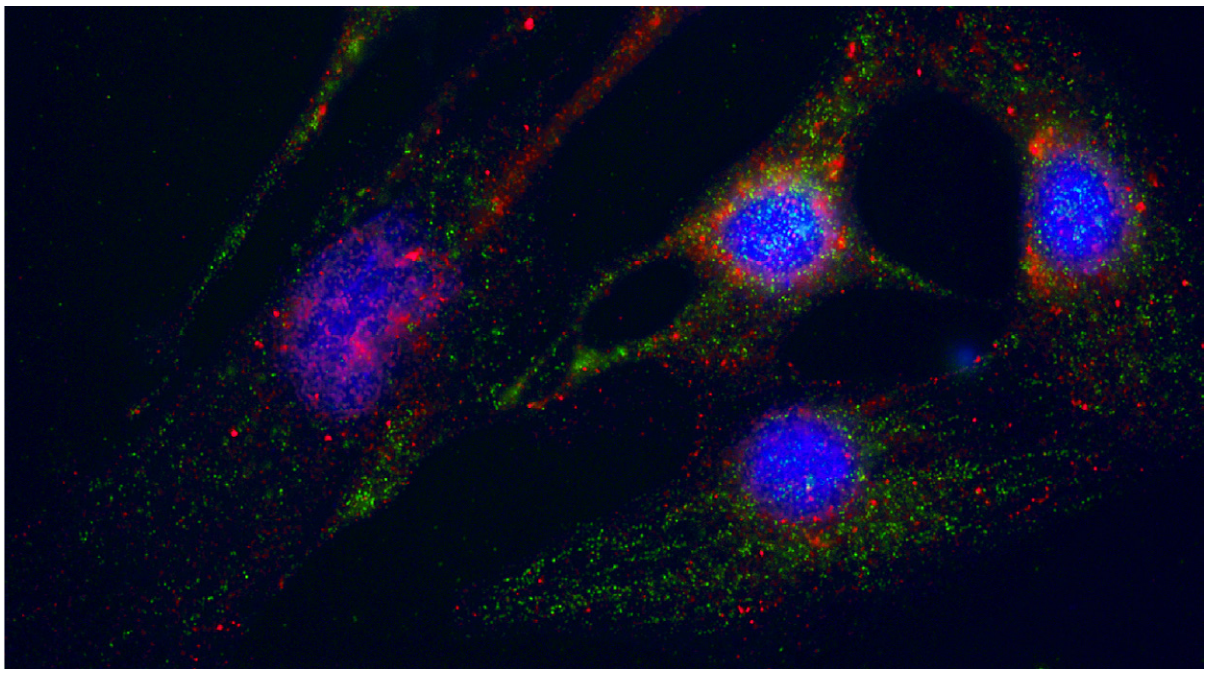
Prof Lea Delbridge

Project Co-supervisor:

Dr Kimberley Mellor

Project Availability:

- PhD
- Master of Biomedical Science



Project 1

Project: Investigating sex differences in heart failure

Heart failure with preserved ejection fraction (HFpEF) accounts for more than 50% of heart failure patients and is particularly prevalent in women. An understanding of the cellular mechanisms underlying HFpEF is limited with no clinical treatments identified. In particular, gender-specific aspects of HFpEF etiology have not been well characterised. There are few animal models of HFpEF currently available and those that are utilised generally investigate male animals only. We have used our unique model of HFpEF to produce preliminary experimental evidence which suggests that the cellular mechanisms underlying this disease are different in males and females. This project will expand and extend these findings to evaluate sex differences in the cellular and molecular mechanisms of HFpEF and aims to identify sex specific therapeutic targets for this disease.

Project Supervisor:

Prof Lea Delbridge

Project Co-supervisor:

Dr Claire Curl

Project Availability:

- PhD
- Master of Biomedical Science

Project: New therapeutic leads in heart failure – developing protein phosphatase directed treatments

Heart failure is a debilitating condition in which the ability of the heart to meet the body's demands for oxygenated blood is compromised. Prognosis is poor, with approximately 50 per cent of patients with heart failure dying within 5 years of diagnosis. There is a clear need for new therapeutic strategies for the treatment of heart failure. Much of the research focus to date has been on the 'kinase' super family of enzymes – which are cardiometabolic 'on' switches. This project will explore the role of a family of proteins known as 'protein phosphatases' which provide the physiological 'off' switch to oppose kinase action. In this project the particular role of selected phosphatase treatments will be explored. The goals are to examine how phosphatases can be protective in suppressing the development of heart failure, and whether phosphatases can be selectively targeted to delay progression of heart failure.

This project will involve work with new 'gene-editing' technology developing experimental models of disease and also involves work with clinical biopsy samples. Students have the opportunity to experience research in the University academic setting in Parkville and also to interact with collaborators at the Baker Heart & Diabetes Institute.

Project Supervisor:

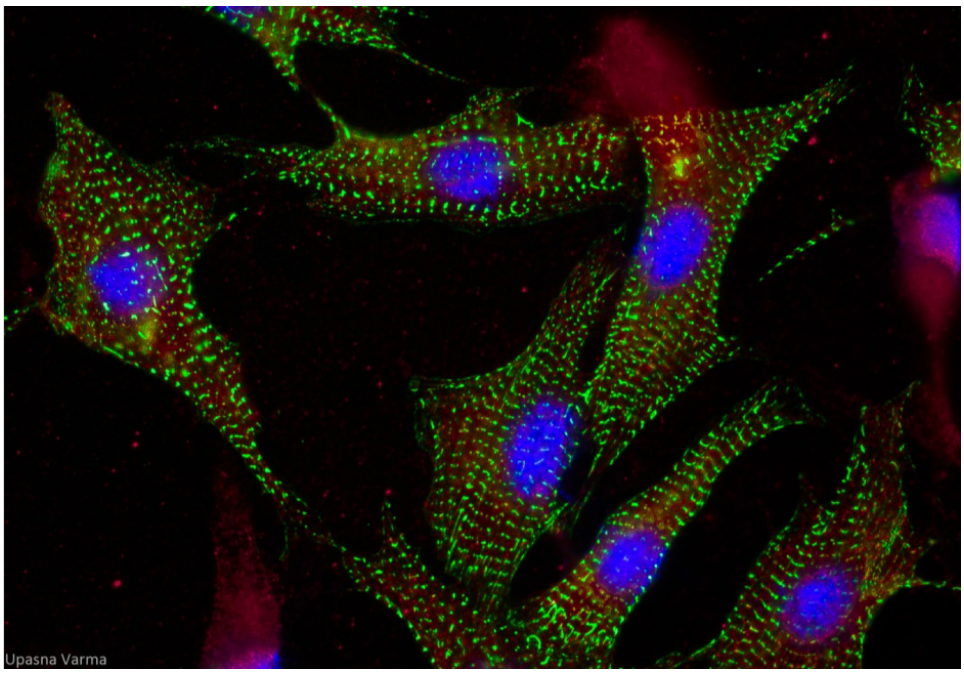
Dr Kate Weeks

Project co-supervisor

Prof Lea Delbridge

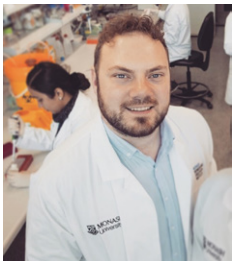
Project Availability:

- PhD
- Master of Biomedical Science



Project 2

Dodd Group



Contact: Dr Garron Dodd
Email: garron.dodd@unimelb.edu.au
Location: Department of Anatomy and Physiology

Metabolic diseases, such as obesity and type-2 diabetes, represents the biggest biomedical challenges of our time. With the ever-increasing metabolic disease epidemic and the insurmountable costs of treating comorbidities (cancer, cardiovascular disease and stroke), there has never been a more desperate need to discover novel pharmacological treatments.

Project: Targeting the Brain to Treat Type-2 Diabetes

Type-2 diabetes is one of the world's fastest-growing conditions, affecting over >9% of the population and costing >$537 billion of world health expenditure. Current therapeutics have limited long term efficacy and confounding side effects. The discovery of effective treatments for type-2 diabetes is identified as an international health priority.

When we eat, insulin is secreted from the pancreas where it travels, via the blood, to signals to neurons in the brain's hypothalamus. Insulin signalling in neurons of the hypothalamus tells our brain to stop eating. This insulin-brain axis is imperative as it keeps blood glucose levels within a safe range.

During the development of type-2 diabetes, neurons in the hypothalamus become encased in an extracellular matrix, which blocks insulin signalling. As a result, insulin can no longer inform the brain that blood sugar levels are too high and type-2 diabetes ensues. Understanding how this extracellular matrix makes neurons insulin resistant and how this can then be targeted by drugs is a critical roadblock in the fight against diabetes.

In this state-of-the-art project, you will use the latest in vivo transgenic approaches including CRISPR-Cas9 genome editing in the brain, stereotaxic surgery and whole brain tissue clearing to genetically dissect out the components of the hypothalamic matrix underlying neuronal insulin resistance. The outcomes of this project will identify novel therapeutic targets to treat neuronal insulin resistance and identify undiscovered disease mechanisms underlying type 2 diabetes.

Project Supervisor:

Dr. Garron Dodd

Project Availability:

- PhD
- Master of Biomedical Science
- Honours

Project: A New Way to Treat Brain Cancer

Project Description: "Glioblastoma multiforme (GBM) is an incurable and highly aggressive brain tumour that universally leads to death. It is the most common primary brain malignancy in adults, accounting for over 50% of intrinsic brain tumours. Unfortunately, GBM has an exceptionally poor prognosis, with an average survival time of less than 14 months, a 5-year survival rate of less than 5%, and a significant decline in the patient's quality of life due to neurological deficits and cognitive impairments. Current treatments for GBM, including surgical resection, chemotherapy, and radiotherapy, are largely ineffective in promoting disease remission and only offer limited extensions of life by a few days or months. With the global incidence of GBM on the rise, there is an urgent need to identify novel disease mechanisms and innovative therapeutic strategies to improve patient outcomes.

Despite the lack of effective treatments for GBM, our laboratory has made an important discovery regarding the expression of a specialized extracellular matrix within GBM. We hypothesize that this matrix promotes tumour growth while hindering the delivery of chemotherapy to target the GBM effectively. Leveraging this knowledge, we have recently developed several small-molecule inhibitors specifically designed to target the specialized extracellular matrix associated with GBM.

In this exciting project, you will have the opportunity to utilize human-relevant pre-clinical models of GBM, along with state-of-the-art neuroscience techniques, to investigate the therapeutic potential of these pioneering "first in class" compounds that target the GBM extracellular matrix. By examining the impact of these compounds on GBM progression, you will contribute to defining their effectiveness as potential therapeutic agents. This research holds great promise in advancing our understanding of GBM and may provide a vital step towards the development of innovative treatment strategies for this devastating disease."

Project Supervisor:

A/Prof Garron Dodd

Project Availability:

- PhD
- Master of Biomedical Science
- Honours

Project: Exercising the Brain to Treat Obesity

Obesity has become one of the most important clinical-epidemiological challenges facing our society. Obesity arises when the energy we intake as food chronically exceeds the energy we expend via exercise. Despite this simplistic overview the mechanisms underlying the development of obesity are incredibly complex.

It is well established that metabolic hormones such as leptin and insulin regulate our appetite and energy expenditure by signalling to neurons in an area of the brain termed the hypothalamus.

During the development of obesity, neurons in the hypothalamus become resistant to the actions of leptin and insulin which results in excessive food intake and attenuated energy expenditure. The development of leptin and insulin resistance within neurons of the hypothalamus is a critical mechanism underlying the development of obesity the development of drugs capable of reinstating leptin and insulin signalling at the forefront of metabolic research.

Physical activity contributes to the prevention and treatment of obesity, not only by increasing energy expenditure but also by modulating appetite and reducing food intake. Exciting new evidence shows that physical activity can re-sensitising hypothalamic neurons to the actions of leptin and insulin however the molecular mechanisms underlying this are not fully understood.

In this exciting project, you will use state of the art proteomic profiling (with space and time resolution) alongside transgenic mouse models of obesity and exercise training to evaluate the molecular mechanisms by which neurons of the hypothalamus become defective in obesity and how exercise restores them. The results of these studies will provide new insights into how exercise regulates neuronal functional, information that will be used to discover novel drug targets to treat obesity.

Project supervisors

Dr Melanie Eckersley-Maslin

Project Co-supervisor:

Dr Katie Fennell

Project Availability:

- PhD
- Master of Biomedical Science
- Honours

Montgomery Group

Contact: Dr Magda Montgomery
Email: magdalene.montgomery@unimelb.edu.au
Location: Department of Anatomy and Physiology
Weblink: go.unimelb.edu.au/u7hr

One major focus of our group is to understand how the liver contributes to metabolic disease - ie. obesity, glucose intolerance and insulin resistance. Non-alcoholic fatty liver disease (NAFLD, fat accumulation in the liver) is found in 70% of obese individuals, with up to 30% of those further progressing to the more severe disease state - non-alcoholic steatohepatitis (NASH). NASH is characterized by liver lipid accumulation and inflammation, hepatocyte ballooning and frequently significant fibrosis. This project will focus on understanding defects in lipid metbolism during the progression of liver disease, with the ultimate aim to identify novel therapeutic appraoches for NASH and fibrosis.

Our group is interested in understanding the development of diabetic heart disease, with a particular focus on changes in mitochondrial function within the heart. We aim to define the metabolic pathways that drive cardiac mitochondrial dysfunction, with the long-term goal to identify new therapeutic angles for the treatment of heart disease.

Understanding dysregulated lipid metabolism in advanced liver disease

Non-alcoholic steatohepatitis (NASH) is characterised by presence of hepatic steatosis (lipid accumulation in the liver), inflammation, and hepatocyte injury, in the absence or presence of hepatic fibrosis, which can further progress to end-stage liver diseases, including liver cancer and cirrhosis, contributing to overall death. Despite this increasing clinical epidemic, there are currently no approved therapies for NASH and liver fibrosis. This is related to our limited understanding of the metabolic adaptations that occur within the liver during the development of NASH. This project will focus on understanding the dysregulation of lipid metbolism during the progression of liver disease, with the ultimate aim to identify novel therapeutic appraoches for NASH and fibrosis.

Project Supervisor:
Dr Magdalene Montgomery

Project Availability:
- Master of Biomedical Science
- Honours

Understanding the contribution of the liver to systemic metabolism and blood glucose control

Non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes are closely linked, yet the pathophysiological mechanisms underpinning this bidirectional relationship remain unresolved. This project will focus on understanding the contribution of dysregulated lipid metabolism in the liver to systemic impairments in blood glucose control, and the identification of novel therapeutic targets for type 2 diabetes.

Primary Supervior:
Dr Magdalene Montgomery

Project Availability:
- Honour
- Masters
- PhD

Parker Group

Contact: Dr Benjamin Parker
Email: ben.parker@unimelb.edu.au
Location: Department of Anatomy and Physiology

The Metabolic Proteomics and Signal Transduction Group is focused on understanding how signal transduction regulates metabolism with the goal of identifying new therapeutic targets to treat disease. We are particularly interested in studying dynamic changes in proteins and their post-translational modifications, and understanding how these are regulated by genetic variants and metabolic insults to ultimately shape cellular physiology. We primarily focus on metabolic tissues such as liver and adipose with a strong emphasis on muscle and bone.

Project: Modulating skeletal muscle signal transduction to treat pre-diabetes

Insulin resistance (or pre-diabetes) is the fastest growing disease in the world and it's estimated >2 million Australians are at risk of developing type-2 diabetes. We urgently need new therapeutic treatments to use in conjunction with diet/exercise to treat these diseases. Insulin resistance is characterised by a major defect in the ability of insulin to promote glucose uptake into skeletal muscle. This results in hyperglycemia and several other diabetic complications. We have identified a series of lead candidates that promote insulin sensitivity and glucose uptake into skeletal muscle. These lead candidates include several kinases and phosphatases that regulate phosphorylation-based signaling pathways.

This project will perform ex vivo functional screening in a series of pre-clinical models to understand how signaling pathways regulate glucose uptake and metabolism. The project will involve a variety of techniques including isotopic tracing of metabolism, phosphoproteomics and biochemistry.

Project Supervisor:
Dr Benjamin Parker

Project Availability:
- PhD
- Master of Biomedical Science
- Honours

Project: Multi-omic analysis and functional genomics of insulin resistance and type-2 diabetes in bone

Bone is more than a structural organ and scaffold for the production of blood cells. Bone tissue is in fact an endocrine organ and plays important roles in the regulation of insulin resistance and development of type-2 diabetes. This project aims to understand how bone regulates whole body metabolism and how insulin regulates bone biology. The project will use mouse and cell models of insulin resistance and perform a variety of assays including proteomics, cell biology and biochemistry. The outcomes may identify new therapeutic targets to treat insulin resistance by targeting bone.

Project Supervisor:
Dr Benjamin Parker

Project Availability:
- PhD
- Master of Biomedical Science
- Honours

Project: Developing novel proteomic methods to study signal transduction

Mass spectrometry â€“ based proteomics is an exciting and rapidly expanding technique to globally sequence and quantify thousands of proteins simultaneously. Furthermore, the technique can characterise new protein modifications that make up important signal transduction pathways. This project will develop a series of new assays to quantify protein post-translational modifications and understand how they change during the development type-2 diabetes. The student will gain hands-on experience in biochemistry, liquid chromatography, tandem mass spectrometry and bioinformatics.

Project Supervisor:
Dr Katherine Drummond

Project Co-supervisor
Prof Anne-Louise Ponsonby

Project Availability:
- PhD
- Master of Biomedical Science
- Honours

Watt Group

Contact: Prof Matthew Watt
Email: matt.watt@unimelb.edu.au
Location: Department of Anatomy and Physiology

Our innovative research program seeks to identify how defects of lipid metabolism and inter-tissue communication cause obesity-related disorders, including type 2 diabetes and non-alcoholic fatty liver disease (NAFLD). We use this information to discover novel targets that can be transitioned to clinical therapeutics. Our research themes are:

1. Understanding how insulin resistance develops in obesity.
2. Understanding how proteins that are secreted by NAFLD / non-alcoholic steatohepatitis (NASH) liver affect metabolism and contributes to the development of type 2 diabetes.
3. Regulation of lipid metabolism: identifying novel proteins that control lipid metabolism and how they are altered in metabolic diseases (e.g. diabetes, cancer).

Project: Discovery of new proteins that lead to the development of type 2 diabetes

A major goal of our research program is to understand how obesity changes liver function and how this contributes to the development of type 2 diabetes. An excessive accumulation of fat in the liver is known as non-alcoholic fatty liver disease (NAFLD) and occurs in 70% of obese individuals, with up to 30% of those individuals progressing to the more severe disease state known as non-alcoholic steatohepatitis (NASH). We aim to understand how proteins termed 'hepatokines' that are secreted by the NAFLD/NASH liver affect metabolism in tissues of the body, and how this contributes to the development of type 2 diabetes.

We have previously used a high-throughput screen to identify several proteins whose secretion is increased in NAFLD and NASH and we now aim to determine whether these proteins affect (1) glucose metabolism and blood glucose control, (2) insulin sensitivity and (3) lipid metabolism in skeletal muscle, liver, adipose tissue and the pancreas. In this project, you will evaluate the effects of newly identified hepatokines on muscle, liver and fat cell metabolism and extend these studies to mouse models of pre-diabetes and diabetes.

Project Supervisor:

Prof. Matthew Watt

Project Availability:

- PhD
- Master of Biomedical Science
- Honours

Project: New ways to improve metabolism: understanding mitochondria and lipid droplet interactions in health and disease

Although many biology textbooks indicate that organelles, such as mitochondria and lipid droplets, are static within cells, recent discoveries have transformed this view and show dynamic interactions between organelles in the same 'neighbourhood'. Mitochondria are critical for generating energy, lipid droplets provide the fuel for mitochondrial energy production and these organelles come into close contact, particularly during metabolically demanding situations. However, we do not know how and why mitochondria are in physical contact with lipid droplets. We aim to test the hypothesis that the inter-organellar interaction of mitochondria and lipid droplets is essential for normal energy metabolism and that this process is dysregulated in metabolic diseases such as obesity and diabetes.

The student in this project will identify novel proteins that are essential for mitochondria-lipid droplet interactions and determine their metabolic consequences. This will be achieved with proteomic profiling (with space and time resolution), by generating knock-out cell lines using state-of-art genetic editing tool CRISPR-Cas9, imaging of cells using super-resolution microscopy and performing detailed assessment of metabolism. The results of these studies will provide new information regarding the regulation of cell metabolism, information that could be harnessed to develop new therapies for metabolic diseases.

Project supervisors

Prof. Matthew Watt

Project Co-supervisor:

Dr. Ayenachew Bezawork-Geleta

Project Availability:

- PhD
- Master of Biomedical Science
- Honours

Project: Chewing the fat: characterisation of protein-protein interactions regulating lipid metabolism

Defective lipid (fat) metabolism is associated with the development of many diseases, including type 2 diabetes, cardiovascular disease and fatty liver disease. Lipids are contained within specialised organelles called 'lipid droplets' and are required for survival. It is known that proteins located on the surface of lipid droplets can regulate lipid synthesis and lipid breakdown. We have recently discovered several novel proteins at the surface of the lipid droplet and the aim of this project is to determine their role in regulating metabolism. This will be achieved by using state-of-the-art protein labelling techniques, confocal microscopy to assess protein-protein interactions and detailed assessment of metabolism. Targeting lipid droplet proteins will provide insight into new treatment strategies for metabolic disease.

Project supervisors

Prof. Matthew Watt

Project Co-supervisor:

Dr. Stacey Keenan

Project Availability:

- PhD
- Master of Biomedical Science
- Honours

Project: Awkward conversations: understanding how exosomes from fatty liver cause metabolic dysfunction

Non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes are common co-morbidities, suggesting there may be communication between these two conditions. Exosomes are small vesicles that contain a variety of proteins, miRNAs, and lipids that can be delivered to peripheral cell types and alter recipient cell function. We have preliminary evidence showing that exosomes secreted by fatty liver differ from healthy control mice, suggesting that changes in exosome secretion might drive metabolic dysfunction in NAFLD. In this project, you will investigate the role of exosomes in regulating metabolism and insulin resistance in cultured cells and mice. These studies will provide valuable new insights into the pathogenesis of metabolic diseases such as type 2 diabetes.

Project supervisors

Prof. Matthew Watt

Project Co-supervisor:

Dr. Paula Miotto

Project Availability:

- Master of Biomedical Science
- Honours

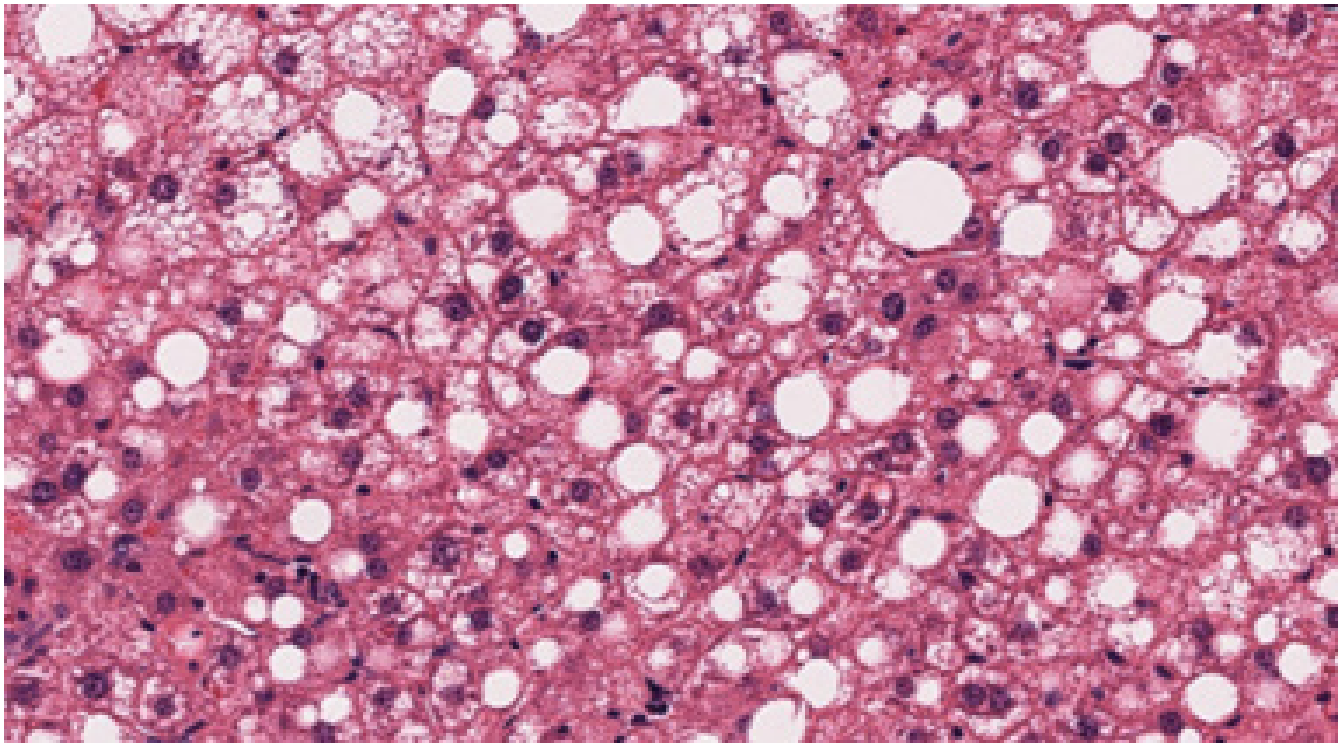


Image showing liver section from a patient with fatty liver disese. Note the abundance of lipid droplets (white circles).

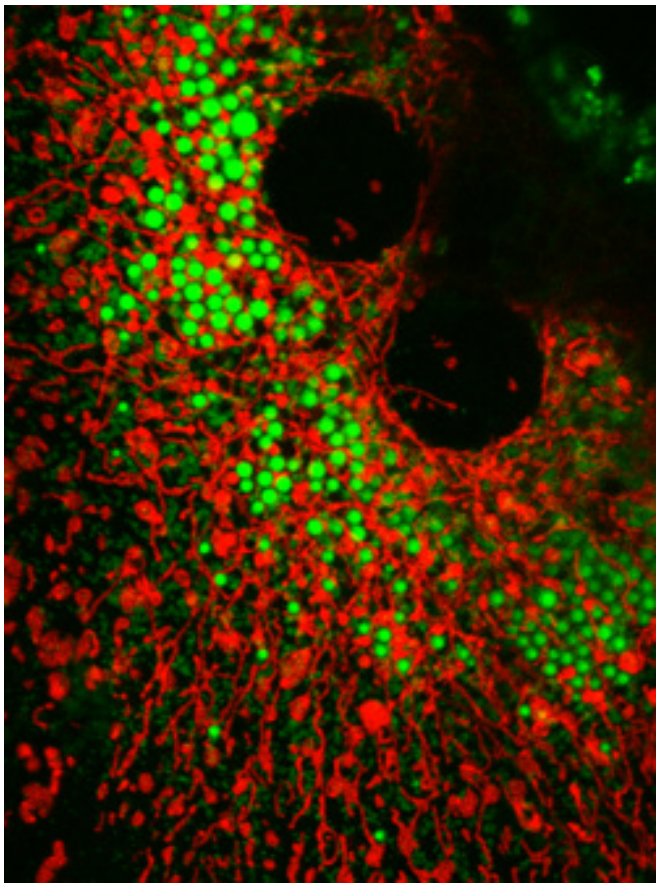


Image showing lipid droplets (green) in close association with mitochondria (red) in liver cells.

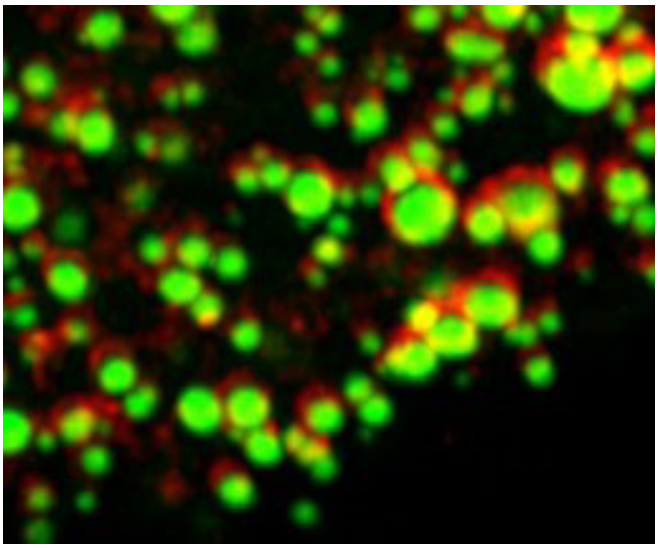
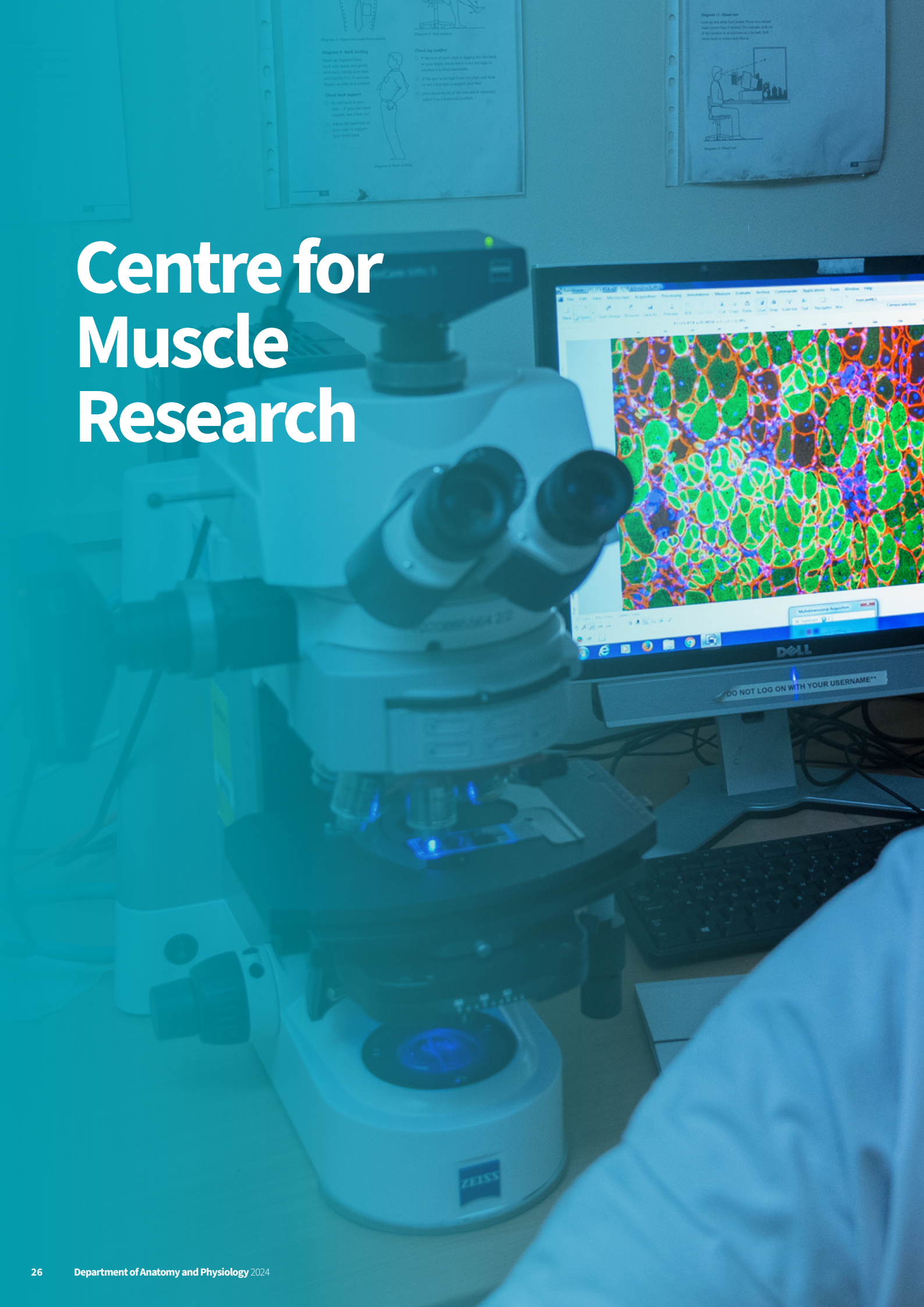


Image of lipid droplets (green) within liver cells in close contact with a protein that regulates lipid metabolism (red).

Centre for Muscle Research



Skeletal muscle is essential for survival. Not only is muscle the vital organ for movement but the diaphragm muscle sustains life by inflating the lungs for breathing. Skeletal muscle is also an endocrine organ that contracts and releases hormones and factors that communicate with other body tissues to sustain life. Skeletal muscle accounts for half a person's body mass yet we take for granted its crucial role in our health and lifestyle.

Many diseases and conditions are linked with changes in muscle structure and function, including: ageing and frailty; cancer; muscle injury, sepsis and other forms of metabolic stress; nerve injury; disuse through inactivity and microgravity; burns; and different forms of muscular dystrophy. These conditions are major health problems globally and contribute to a large burden of disability and suffering. Tackling these muscle-related health conditions requires a coordinated research effort from discovery biology to understand disease mechanisms and translational approaches to take these discoveries from bench to the clinic. Researchers in the Centre for Muscle Research seek to understand the mechanisms that regulate muscle growth, wasting and metabolism, and to develop new approaches for preventing or treating muscle related conditions, utilising the latest techniques in biology and biomedicine.

We also consider skeletal muscle in the context of other diseases, such as heart and cardiovascular diseases, cancer and osteoporosis. We are interested in understanding muscle development and growth, injury and repair, studying the biology and metabolism of muscle stem cells and their commitment to becoming functional muscle fibres. Our researchers design, manufacture and utilise viral vectors to alter gene expression in mouse models of disease and interrogate cellular mechanisms of muscle adaptation, techniques that provide a unique combination of speed, precision and efficacy not achieved through other approaches. The Centre for Muscle Research offers a wonderful training environment for studying muscle biology in health and disease and exceptional career-training opportunities for Honours, Masters and Ph.D. students.

Basic & Clinical Myology

Contact: Prof Gordon Lynch
Email: gsl@unimelb.edu.au
Location: Department of Anatomy and Physiology

Project: Therapeutic potential of skeletal muscle plasticity and slow muscle programming for muscular dystrophy

Duchenne muscular dystrophy (DMD) is a devastating, life-limiting, muscle disease that causes progressive, severe muscle wasting in boys and young men. There is currently no cure. A potential therapy may come from altering muscle phenotype based on slower, more oxidative muscle fibres being better protected from the dystrophic pathology than faster, more glycolytic muscle fibres. Muscle plasticity can be achieved through exercise and/or through well described pharmacological approaches like activation of AMP-activated protein kinase (AMPK). Physical activity has many beneficial effects on muscle health but unfortunately many patients simply cannot exercise, especially those with DMD. Modulating muscle activity patterns through low-frequency electrical stimulation (LFS) protocols could mimic the benefits of exercise and promote a slow muscle phenotype. No studies evaluating the therapeutic merit of LFS have been conducted on the accepted mouse models of DMD nor have they determined whether muscle wasting can be attenuated or reversed. Similarly, no studies have examined the therapeutic merit of LFS in conjunction with AMPK activators. These studies are essential for enhancing the clinical translation to improve patient quality of life.

Project Supervisor:
Prof. Gordon Lynch

Project Co-supervisor:
Dr. Justin Hardee

Project Availability:
- PhD
- Master of Biomedical Science
- Honours

Project: Metabolic reprogramming in skeletal muscle stem cells

Recent work has uncovered an essential role for metabolism in the generation of the building blocks (nucleotides, phospholipids, and amino acids) required by rapidly dividing cells. Additionally, the metabolite balance of both stem and differentiated cells has been found to directly influence the epigenome through post-translational modifications of histones, DNA and transcription factors and therefore has important implications for stem cell activation and proliferation. The overall goal of research into the link between metabolism and stem cell identity is to improve stem cell transplantation and regenerative medicine, and stable ex vivo expansion of stem cells. This project will utilise cutting-edge techniques such as RNAseq, metabolomics and imaging mass-spectrometry, and will have broad application in the fields of regenerative medicine, synthetic biology and cellular agriculture (the growth of so-called "clean-meat").

Project Supervisor:
Prof. Gordon Lynch

Project Availability:
- PhD
- Master of Biomedical Science
- Honours

Project: Interrogating the therapeutic potential of slow muscle programming in cancer

Project Description: Skeletal muscle is comprised of diverse fibre types that differ in size, metabolic and contractile properties; classically referred to as either ‘slow, oxidative’ or ‘fast, glycolytic’. These properties are not fixed but can change in response to imposed demands, a process known as ‘plasticity’. Understanding the biological mechanisms regulating fibre phenotype and the adaptive response across muscles of varying phenotypes has not been fully resolved. Addressing these research gaps may also identify potential therapeutic targets to improve quantity and quality of life across many disease conditions. The objectives of this project are to: 1) understand the biological mechanisms regulating fibre size, phenotype and plasticity; and 2) whether modifying skeletal muscle attributes can protect against injury and disease. This project will utilise genetic, pharmacological and lifestyle approaches to interrogate the molecular, metabolic and contractile properties of fast and slow muscles in a variety of healthy and pathological states; including but not limited to muscular dystrophies, cancer cachexia, muscle injury and repair, and ageing.

Primary Supervisor:
Prof Gordon Lynch

Co-supervisor:
Dr Justin Hardee

Project Availability:
- PhD
- Honours
- Master of Biomedical Science

Project: Establish the effect of glycine/serine metabolism on skeletal muscle cell growth.

Project Description: Skeletal muscle cell proliferation and growth require the production of building blocks for new cellular components (proteins, lipids and nucleic acids) as well the maintenance of cellular redox status. Observations in other cells suggest that the metabolism of the amino acid L-serine and its intermediate glycine can provide carbon units that satisfy many of these requirements. However, the cellular demand for L-serine is much greater than its uptake suggesting that the de novo production of L-serine is of critical importance to sustain cellular growth. Surprisingly, to date no detailed investigation of the role of L-serine biosynthesis in skeletal muscle has been performed and whether L-serine can support the production of biomass in growing muscle cells remains to be established.

Project Supervisor:

Prof Gordon Lynch

Project Co-Supervisor:

Dr Marissa Caldow

Project Availability:

- Honours
- PhD
- Masters of Biomedical Science

Project: Characterising the pathways responsible for ICU-acquired weakness

Project Description: Muscle wasting is the most common complication of critical illness, occurring in 25-50% of patients. The extent of wasting is determined by the severity of organ failure and lung injury, however, a loss of 20-30% of muscle mass over the first 10 days in ICU is not uncommon. ICU patients generally have increased muscle protein breakdown relative to muscle protein synthesis, leading to a net catabolic state and rapid loss of muscle mass and function. To allow the development of novel and effective treatments to attenuate muscle wasting in ICU patients it is important to identify the signalling pathways and proteins that drive this catabolic state. This project uses animal-based experiments and analyses of muscle biopsies from ICU patients to comprehensively test these mechanisms. Findings from this project will enhance our knowledge about the regulation of skeletal muscle mass during critical illness and will aid in the further development of treatment strategies

Project Supervisor:

Prof Gordon Lynch

Project Co-Supervisor:

Dr Marissa Caldow

Project Availability:

- Honours
- PhD
- Masters of Biomedical Science

Ruparelia Group

Contact: Dr Avnika Ruparelia
Email: avnika.ruparelia@unimelb.edu.au
Location: Medical Building

The Ruparelia lab is investigating the fundamental biology of muscle wasting disorders such as sarcopenia, which is the age-related decline in muscle mass and function, and genetic conditions such as Duchenne muscular dystrophy - examining processes such as muscle fiber atrophy and growth, muscle stem cell dynamics, muscle regeneration, and metabolism. We not only use the unique advantages of the zebrafish model, but also uses a new experimental system – that of the African killifish, whose extremely short lifespan makes it an attractive model for ageing research.

Project: Muscle stem cells in muscular dystrophy: a role of lipid metabolism

Project Description: Muscular dystrophies have one of the highest burdens of disease, and yet, there is currently no cure for this devastating group of muscle wasting disorders. Therefore, using the advantages of the zebrafish model system combined with genetic approaches, confocal microscopy, immunofluorescence techniques and live imaging, we aim to identify novel therapeutic strategies for the treatment of muscular dystrophy, focusing on lipid metabolism. Importantly, in addition to targeting the muscle cell, we will also correct defects in the muscle stem cell, which is something that has previously not been done. This will not only prevent the loss of muscle cells but also improve the repair and regeneration of damaged muscle thereby improving muscle function in patients with muscular dystrophy.

Project Supervisor:
Dr Avnika Ruparelia

Project Availability:
- Honours
- Master of Biomedical Science
- PhD

Project. Understanding the mechanisms regulating sarcopenia using zebrafish

Project Description Sarcopenia, the age-related decline in muscle mass and function, places a great burden on the health care system. Despite this, very little is known about the molecular pathways that drive this process. Using the advantages of the zebrafish model system combined with confocal microscopy and immunofluorescence techniques, this project will examine the role of the atrophy regulating gene, murf1, in promoting sarcopenia.

Project Supervisor:
Dr Avnika Ruparelia

Project Availability:
- Honours
- Master of Biomedical Science
- PhD

Project. Identifying disease pathogenesis of RYR1 variants

Project Description Mutations in the sarcoplasmic reticulum calcium release channel, Ryanodine receptor 1 (RYR1), result in the most common non-dystrophic congenital myopathy. Given the large size of this gene, there are a significant numbers of potentially disease-causing variants which do not reach the current threshold for definitive genetic diagnosis. Using the advantages of the zebrafish model system combined with confocal microscopy, immunofluorescence techniques and live imaging, this project will determine the pathogenicity of RYR1 variants of uncertain significance.

Project Supervisor:
Dr Avnika Ruparelia

Project Availability:
- Honours
- Master of Biomedical Science
- PhD

Basic & Clinical Myology

Contact: Dr Justin Hardee
Email: justin.hardee@unimelb.edu.au
Location: Department of Anatomy and Physiology

Project: Understanding the plasticity of skeletal muscle in health and disease.

Skeletal muscle is comprised of diverse fibre types that differ in size, metabolic and contractile properties; classically referred to as either 'slow, oxidative' or 'fast, glycolytic'. These properties are not fixed but can change in response to imposed demands, a process known as 'plasticity'. Understanding the biological mechanisms regulating fibre phenotype and the adaptive response across muscles of varying phenotypes has not been fully resolved. Addressing these research gaps may also identify potential therapeutic targets to improve quantity and quality of life across many disease conditions. The objectives of this project are to: 1) understand the biological mechanisms regulating fibre size, phenotype and plasticity; and 2) whether modifying skeletal muscle attributes can protect against injury and disease. This project will utilise genetic, pharmacological and lifestyle approaches to interrogate the molecular, metabolic and contractile properties of fast and slow muscles in a variety of healthy and pathological states; including but not limited to muscular dystrophies, cancer cachexia, muscle injury and repair, and ageing.

Project Supervisor:
Dr. Justin Hardee

Project Co-supervisor:
Prof. Gordon Lynch

Dr. Rene Koopman

Project Availability:

- PhD
- Master of Biomedical Science
- Honours

Basic & Clinical Myology

Contact: Dr Kristy Swiderski
Email: kristys@unimelb.edu.au
Location: Department of Anatomy and Physiology

Project: Investigating the Dystrophin-Glycoprotein Complex to protect muscles from wasting conditions

The dystrophin-glycoprotein complex (DGC) is a multi-protein structure required to maintain integrity of the muscle fibre membrane and to transmit force, by linking the actin cytoskeleton with the extracellular matrix. Importantly, we and others have shown the DGC also plays a critical role in the signalling mechanisms that maintain muscle homeostasis and membrane localisation of dystrophin is perturbed in muscles wasting as a consequence of cancer cachexia, sepsis, unloading, denervation and advanced ageing, which are all associated with low level, chronic inflammation.Identifying therapeutic approaches to restore the DGC at the muscle fibre membrane is essential for improving clinical outcomes for patients whose muscles are wasting and seemingly unresponsive to other treatments. This project will test the hypothesis that loss of DGC integrity at the fibre membrane is implicated in multiple wasting conditions and that post-translational modification modulates these DGC interactions to preserve and protect muscles in different muscle wasting states.

Project Supervisor:
Dr. Kristy Swiderski

Project Co-supervisor:
Prof. Gordon Lynch

Assoc. Prof Paul Gregorevic

Project Availability:

- PhD
- Master of Biomedical Science
- Honours

Metabolic Proteomics and Signal Transduction

Contact: Dr Benjamin Parker
Email: ben.parker@unimelb.edu.au
Location: Department of Anatomy and Physiology
Website: go.unimelb.edu.au/3r5i

The Metabolic Proteomics and Signal Transduction Group is focused on understanding how signal transduction regulates metabolism with the goal of identifying new therapeutic targets to treat metabolic diseases. We primarily focus on metabolic tissues such as brain, liver, adipose, and muscle. Our research integrates physiology with systems biology techniques such as proteomics to understand how metabolic tissues develop, how they are regenerated, how they are affected by physical activity, how defects and genetic variants contribute to insulin resistance, and the identification and development of novel therapeutics.

Project: Developing novel proteomic methods to study signal transduction

Mass spectrometry â€“ based proteomics is an exciting and rapidly expanding technique to globally sequence and quantify thousands of proteins simultaneously. Furthermore, the technique can characterise new protein modifications that make up important signal transduction pathways. This project will develop a series of new assays to quantify protein post-translational modifications and understand how they change during the development type-2 diabetes. The student will gain hands-on experience in biochemistry, liquid chromatography, tandem mass spectrometry and bioinformatics.

PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science
- Honours

Project: Multi-omic analysis and functional genomics of insulin resistance and type-2 diabetes in bone

Bone is more than a structural organ and scaffold for the production of blood cells. Bone tissue is in fact an endocrine organ and plays important roles in the regulation of insulin resistance and development of type-2 diabetes. This project aims to understand how bone regulates whole body metabolism and how insulin regulates bone biology. The project will use mouse and cell models of insulin resistance and perform a variety of assays including proteomics, cell biology and biochemistry. The outcomes may identify new therapeutic targets to treat insulin resistance by targeting bone.

Project Supervisor:

Dr Benjamin Parker

PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science
- Honours

Project: Modulating skeletal muscle signal transduction to treat pre-diabetes

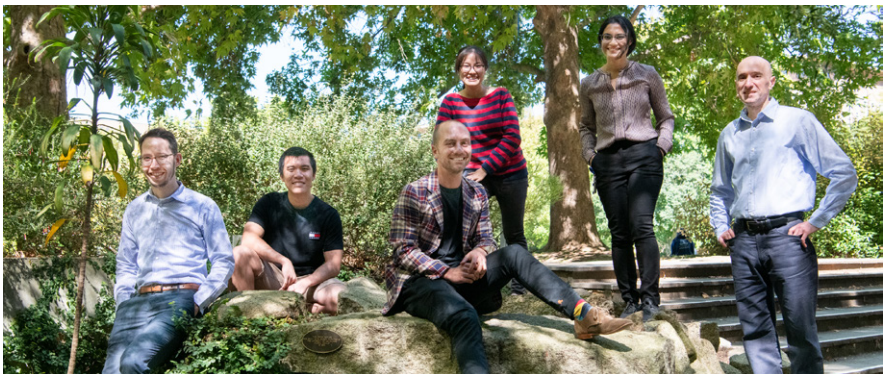
Insulin resistance (or pre-diabetes) is the fastest growing disease in the world and it's estimated >2 million Australians are at risk of developing type-2 diabetes. We urgently need new therapeutic treatments to use in conjunction with diet/exercise to treat these diseases. Insulin resistance is characterised by a major defect in the ability of insulin to promote glucose uptake into skeletal muscle. This results in hyperglycemia and several other diabetic complications. We have identified a series of lead candidates that promote insulin sensitivity and glucose uptake into skeletal muscle. These lead candidates include several kinases and phosphatases that regulate phosphorylation-based signaling pathways. This project will perform ex vivo functional screening in a series of pre-clinical models to understand how signaling pathways regulate glucose uptake and metabolism. The project will involve a variety of techniques including isotopic tracing of metabolism, phosphoproteomics and biochemistry.

Project Supervisor:

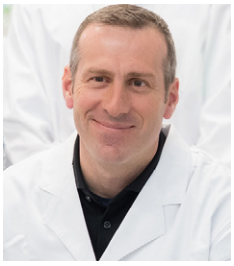
Dr Benjamin L. Parker

Project Availability:

- PhD
- Master of Biomedical Science
- Honours



Muscle Research and Therapeutics



Contact: A/Prof Paul Gregorevic
Email: pgre@unimelb.edu.au
Location: Department of Anatomy and Physiology

Project: Exploring new roles for the TGFβ signalling network as a cause of skeletal muscle disorders, and a target for new muscle therapeutics.

The Transforming Growth Factor β (TGFβ) signalling network is one of the most important regulators of processes associated with skeletal muscle development, adaptation, and repair. However, many questions remain as to how this network is regulated in skeletal muscle in health and disease, how it controls processes that determine skeletal muscle characteristics, and how best to control network elements to prevent/treat muscle conditions. Combining gene delivery-based methods with cell culture and animal models and analyses of gene expression and protein regulation, this research theme seeks to examine novel processes that control the TGFβ network in skeletal muscle and determine how unique components of the TGFβ network control skeletal muscle structure and function. These discoveries will help to develop novel strategies for preventing/treating the loss of skeletal muscle mass and strength associated with disease and advancing age.

Project Supervisor:
A/Prof Paul Gregorevic

Project Co-supervisor:
Dr Craig Goodman

Project Availability:
- PhD
- Master of Biomedical Science
- Honours

Project: Unravelling the mysteries of E3 ubiquitin ligase biology as a regulator of skeletal muscle in health and disease.

Regulation of muscle size and function impacts on all aspects of human health and well-being. From performance on the sports-field, to regulation of whole-body metabolism, and independence in aging. A large family of genes known as E3 ubiquitin ligases are paramount in regulation of muscle homeostasis. Changes in the activity of specific members can provoke muscle frailty and wasting, whilst others promote growth and function. Skeletal muscle expresses over 250 E3 ubiquitin ligases, yet only a handful have been characterised. This research program is investigating which E3 ligases have important functions in muscle health and disease. The projects focus on charting novel E3 ubiquitin ligases, understanding how they regulate muscle size and function, and developing therapeutically relevant methods to control their activity.

Project Supervisor:
A/Prof Paul Gregorevic

Project Co-supervisor:
Dr Craig Goodman

Project Availability:
- PhD
- Master of Biomedical Science
- Honours

Project: Developing innovative animal and human cell models to study and treat muscular dystrophies.

Many neuromuscular disorders remain poorly studied and without adequate therapies due to a lack of suitable models in which to study mechanisms and test possible interventions. This research program combines novel gene- and cell-based approaches to generate new in vitro and in vivo models of neuromuscular disorders. Characterisation and manipulation of these new model systems will enable us to a) study the underlying mechanisms of action associated with muscle disease and b) devise novel much-needed therapeutic strategies for these conditions.

Project Supervisor:

A/Prof Paul Gregorevic

Project Co-supervisor:

Dr. Kevin Watt

Project Availability:

- PhD
- Master of Biomedical Science
- Honours

Project: Learning from skeletal muscle to treat cancer.

Patients with cancer frequently succumb to complications arising from cachexia - a condition characterised by debilitating loss of functional muscle mass, and adipose tissue. Projects within this theme are examining the mechanisms involved in the development of cachexia, in the hopes of helping to develop new therapeutic strategies. Patients with cancer also frequently succumb to complications arising from metastasis - the spread of tumour cells to other sites distant from the tissue of origin. However, the colonisation of metastatic cancers within muscle is remarkably infrequent, and the mechanisms underlying these discrepancies between muscle and other tissues remain unclear. Projects within this theme will examine why skeletal muscles are resistant to metastatic cancers, to identify new strategies for preventing and treating the development and progression of metastatic cancers.

Project Supervisor:

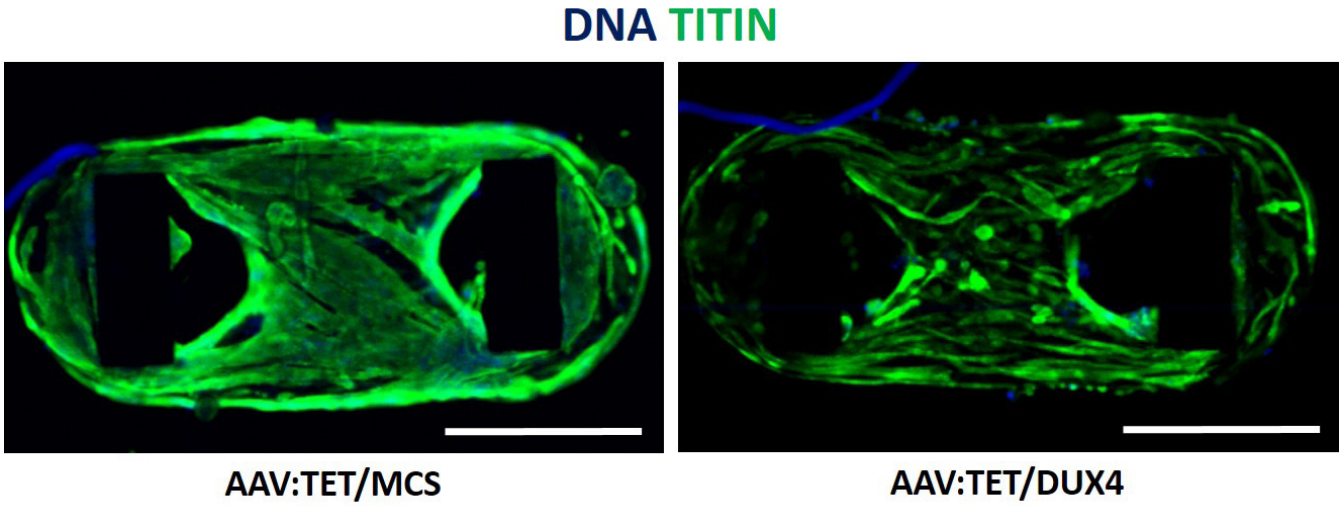
A/Prof Paul Gregorevic

Project Co-supervisor:

Dr. Rachel Thomson

Project Availability:

- PhD
- Master of Biomedical Science
- Honours



Crouch Group

Contact: A/ Prof Peter Crouch
Email: pjcrouch@unimelb.edu.au
Location: Department of Anatomy and Physiology

Assoc. Prof. Crouch's team investigates neurodegenerative diseases of the central nervous system such as motor neuron disease and multiple sclerosis. Our primary interests are elucidating the cellular mechanisms that lead to neuronal death and assessment of putative neuroprotective therapeutic interventions. We utilise models of disease that span in vitro and in vivo paradigms and we also examine human, disease-affected central nervous system tissue.

Project: Muscle-directed gene t herapy as an adjuvant to neuroprotection: Targeting both ends of the dysfunctional nerve-muscle axis to treat motor neurone disease.

Project Description: Amyotrophic lateral sclerosis (ALS), the most common form of motor neuron disease, is an aggressive and fatal neurodegenerative condition. Effective treatments do not exist and most patients die <3 years after diagnosis. The unequivocal cause is deterioration of motor neurons, making neuroprotection an essential requirement. The debilitating physical symptoms of ALS, however, exemplify the major roles that muscle wasting and diminished strength play in burden of disease before death. As skeletal muscle is a highly adaptive and regenerative tissue responsive to diverse muscle-stimulating agents, this opens additional opportunity for targeted treatment. But muscle-stimulating agents have to date failed to provide lasting effects in ALS because their efficacy is blunted by denervation. This project addresses the previously untested possibility that stimulating muscle growth and strength can be beneficial in treating ALS provided the muscle-directed treatments are used as adjuvants to agents that are neuroprotective.

Project Supervisor:
A/Prof Peter Crouch

Project Co-supervisor:
Dr Rachel Thomson
Prof Paul Gregorevic
Dr Jeffrey Liddell

Project Availability:
- M.Phil/PhD
- Honours
- Master of Biomedical Science

Project: Improving CNS copper availability to mitigate permanent neurological disability in progressive cases of multiple sclerosis.

Project Description: Multiple sclerosis (MS) is a debilitating disease of the central nervous system (CNS). Most cases involve intermittent immunological responses with cyclic phases of symptom relapse-remittance. Good treatments exist for these cases via anti-inflammatory and immunomodulatory drugs. The more debilitating cases of MS, however, involve an accumulation of permanent neurological disability due to the involvement of neurodegeneration. There is a dearth of treatments for these cases because the cellular pathways underpinning permanent neurological disability remain poorly defined and evidence is lacking for therapeutic targets. This project involves examination of a novel pathway to neuronal death in multiple sclerosis with opportunity for therapeutic intervention.

Project Supervisor:
A/Prof Peter Crouch

Project Co-supervisor:
Dr Jeffrey Liddell

Project Availability:
- M.Phil/PhD
- Honours
- Master of Biomedical Science

Project: Multiomic interrogation of patient-derived neurotoxic glia.

Project Description: In motor neuron disease (MND), the normally supportive glial cells in the central nervous system become corrupted and toxic to motor neurons. We have discovered a novel pathway that can model this aberrant disease function of glial cells when the cells are grown in culture. Importantly, we have identified that this pathway is present in human cases of MND and appears to play a functional role in determining disease outcomes. This project will involve examination of cells grown in culture to further elucidate this cell death pathway. We will use multiple advanced approaches to thoroughly characterise these cells and their interactions in order to determine how they kill neurons.

Project Supervisor:

Dr Jeffrey Liddell

Project Co-supervisor:

A/Prof Peter Crouch

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science

Sensory Neuroscience

Fletcher Group

Contact: Prof Erica Fletcher
Email: elf@uniemlb.edu.au
Location: Department of Anatomy and Physiology
Website: go.unimelb.edu.au/o65i

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:

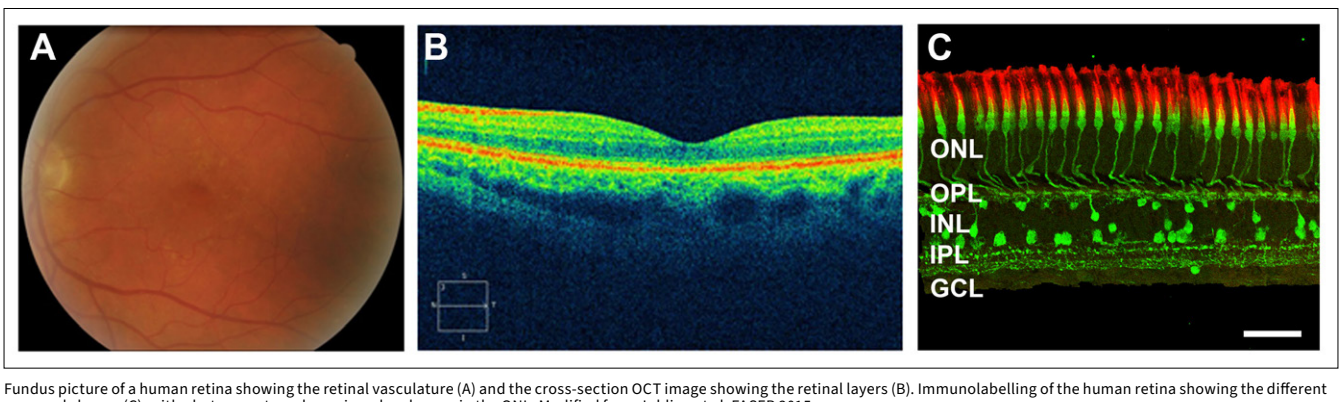
Dr Kristan Vessey

Project Co-supervisor:

Dr Andrew Jobling
Prof Erica Fletcher

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science



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.

Project: Identification of inflammatory factors that lead to retinal swelling

Project Description: The eye is a delicate organ that needs to maintain an immune privileged environment. Uveitis is an inflammation of the eye that if left untreated can lead to blindness. It can be an acute or chronic disease that is classified according to the predominant site of inflammation (anterior, intermediate, posterior, or panuveitis). One concerning outcome of this disease is the development of uveitic macular oedema (retinal swelling) where inflammation leads to the accumulation of fluid within retina. This project will explore the factors that arise from the inflammatory response and whether they cause an alteration in retinal fluid movement. You will use retinal explant culture, immunohistochemistry, cell volume measurement and molecular biology to determine the key mediators of uveitic macular oedema. There is also an opportunity to compare these culture-based effects to clinical samples.

Primary Supervisor:
Dr Andrew Jobling

Co-supervisor:
A/Prof Lyndell Lim

Project Availability:
- M.Phil/PhD
- Honours
- Master of Biomedical Science

Project: Diet-induced mechanisms involved in diabetic retinopathy and macular oedema

Project Description: 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 retinopathy and oedema results from changes in neurons, glia and blood vessels. In type II diabetes, the role of diet has a significant impact on the associated pathology. In preclinical models, this project will use immunohistochemistry, molecular biology and in vivo imaging techniques to examine the changes in retinal structure as a result of prolonged high fat diets. Understanding these diet-induced changes is critical to explaining the retinal pathology that develops during type II diabetes.

Primary Supervisor:
Prof Erica Fletcher

Co-Supervisor:
Dr Andrew Jobling

Project Availability:
- M.Phil/PhD
- Honours
- Master of Biomedical Science

Project: Pharmacological and laser therapies for age related macular degeneration

Project Description: 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 Andrew Joblingi

Co-Supervisor
A/Prof Lyndell Lim
Prof Erica Fletcher

Project Availability:
- Honours
- Master of Biomedical Science
- PhD

Ivanusic Group

Contact: A/ Prof Jason Ivanusic
Email: j.ivanusic@unimelb.edu.au
Location: Department of Anatomy and Physiology
Website: go.unimelb.edu.au/k65i

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:
A/Prof Jason Ivanusic

Project Co-supervisor:
Dr Michael Morgan

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science

Mazzone Group

Contact: Prof Stuart Mazzone
Email: stuart.mazzone@unimelb.edu.au
Location: Department of Anatomy and Physiology

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

Project Availability:
- M.Phil/PhD
- 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

Project Availability:
- M.Phil/PhD
- Honours
- Master of Biomedical Science

Wilkinson-Berka Group

Contact: Prof Jennifer Wilkinson-Berka
Email: Jennifer.wilkinsonberka@unimelb.edu.au
Location: Department of Anatomy and Physiology

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:

Prof Jennifer Wilkinson-Berka

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science

Systems Neuroscience

Bornstein Group

Contact: Prof Joel Bornstein
Email: j.bornstein@unimelb.edu.au
Location: Department of Anatomy and Physiology

Our major research interests are the neural mechanisms and circuits that control intestinal motor functions underlying the digestive process, including both muscle movement and the secretion of water and salt by the mucosa, and how these are disturbed by bacterial toxins.

This work involves experimental methods ranging from electrophysiological analysis of synaptic transmission in reflex pathways, to immunohistochemical analysis of enteric neural circuits, to measurements of intestinal movements and secretions both in vitro and in vivo and computer simulation of the networks of neurons that mediate these functions. Much of this work, especially that involving interactions between intestinal movements and secretion, is carried out in close collaboration with Dr Tor Savidge of Baylor College of Medicine in Texas. Other international collaborations include a consortium led by Professor Marthe Howard (University of Toledo, Ohio) and funded by NIH whose goal is a predictive anatomical map of the enteric nervous system.

Project: Mechanisms underlying synaptic transmission in the enteric nervous system

Transmission between enteric neurons is an essential therapeutic target for many gastrointestinal diseases, but the molecular mechanisms are not clearly established. In this project, key molecules and the dynamic properties of enteric synapses will be identified using immunohistochemistry and calcium imaging to determine how these molecules participate in transmission.

Project Supervisor:
Prof Joel Bornstein

Project Availability:
- Master of Biomedical Science
- Honours

Project: Reproductive cycle dependent plasticity within the enteric nervous system

We have recently found that enteric neural circuits that control gut function change their properties according to the stages of the reproductive cycle in mice. These changes include changes in the neurochemical phenotype of myenteric neurons and appear to depend on circulating estrogens. In this project, you will investigate whether rapid changes in the phenotype of enteric neurons are associated with changes in function using immunohistochemistry, calcium imaging and functional analysis.

Project Supervisor:
Prof Joel Bornstein

Project Availability:
- Master of Biomedical Science
- Honours

Project: Role of bacterially generated GABA in antibiotic associated diarrhoea

Antibiotic treatments frequently produce diarrhoea as a major side effect, and this can be life threatening. We have data indicating that antibiotic treatments that cause antibiotic associated diarrhoea change the gut microbiome so that it produces large amounts of the neurotransmitter GABA. In this project, you will investigate the chronic effects of bacterially derived GABA to identify how this transmitter affects diarrhoeal disease.

Project Supervisor:
Prof Joel Bornstein

Project Availability:
- Master of Biomedical Science
- Honours

Project: Impact of early life antibiotics on the nervous system of the gut and host physiology

Exposure to antibiotic during critical developmental windows have been linked to increased susceptibility to several diseases, including gastrointestinal and metabolic disorders later in life. We have found in mice that exposure to antibiotics early in life during the neonatal period, and in utero (via the female dam) disrupts the developing microbiota, nervous system of the gut and host metabolism. This project will provide critical insights into how antibiotics impacts host physiology, which will aid in elucidating potential circumventive measures for the unwanted side-effects of antibiotic therapy.

Project Supervisor:

Dr Jaime Foong

Project Co-supervisor:

Prof Joel Bornstein

Project Availability:

- Honours
- Master of Biomedical Science

Project: Development of a functional Enteric Nervous System

Proper development of the Enteric Nervous System (ENS) is essential for regulating vital gastrointestinal functions. However, the development of a functioning ENS is still unclear. This project will use advanced microscopy and a robust method of measuring dynamic activity and neurotransmission of the developing enteric circuitry by employing mice in which enteric neurons express a genetically encoded calcium indicator. Findings from this study will elucidate factors that affect maturation of synaptic transmission within the ENS.

Project Supervisor:

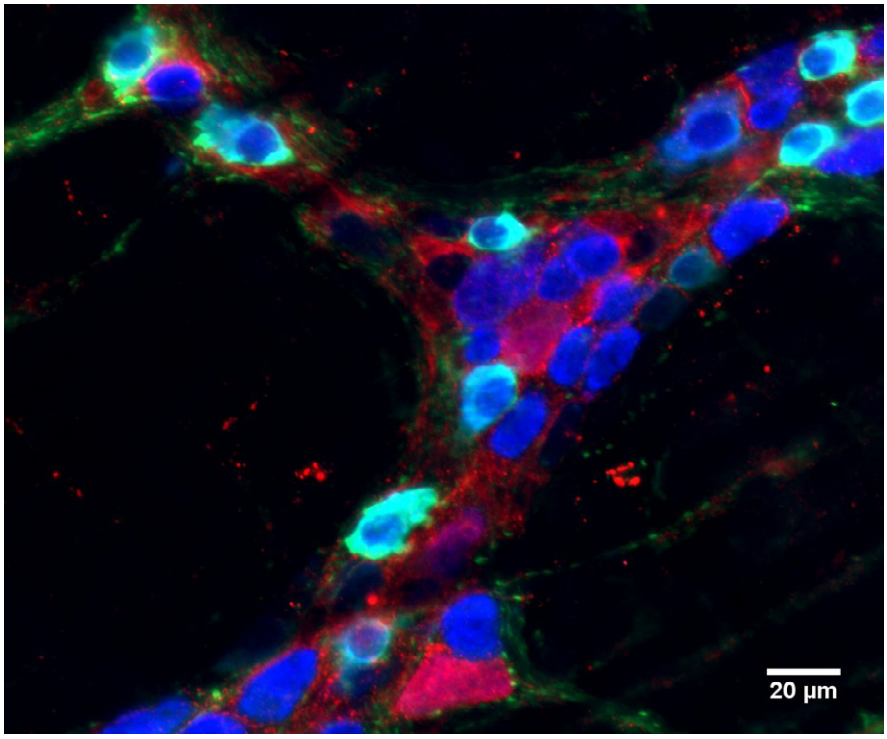
Dr Jaime Foong

Project Co-supervisor:

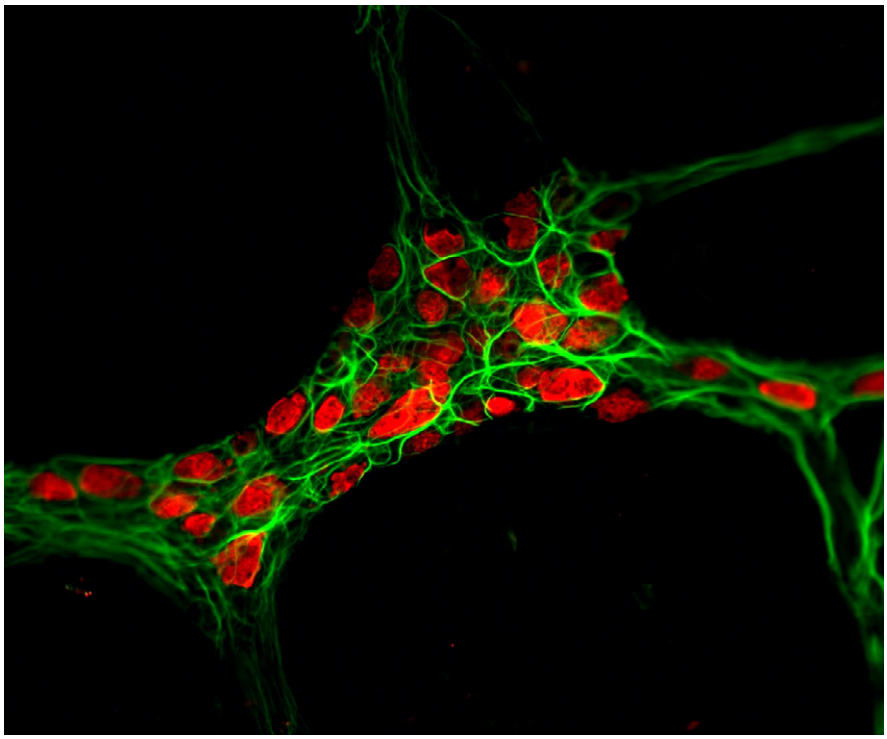
Prof Joel Bornstein

Project Availability:

- Honours
- Master of Biomedical Science



Project 1



Project 2

Central Cardiorespiratory Group

Contact: Dr Mariana Melo
Email: mariana.del@unimelb.edu.au
Location: Department of Anatomy and Physiology

The Central Cardiorespiratory Regulation group is focused on understanding how neural circuits generate complex behaviors. We use sophisticated optogenetic and chemogenetic approaches to address these questions, and develop novel optogenetic and chemogenetic methods where required. This makes it possible to begin unravelling the incredible complexity of the mammalian brain. We are particularly interested in elucidating the neural mechanisms and circuits that control cardiovascular (blood pressure, heart rate) and respiratory system during physiological conditions and their role on the development of pathological state.

Project: Using optogenetics to unravel the interaction between heart rate variability and emotions

Our heart rate (HR) might appear to be constant, but is subject to substantial modulation, resulting in complex variability. One of the most obvious modulations is in phase with the respiratory cycle and is termed respiratory sinus arrhythmia (RSA). Currently there is a lot of interest in HR variability (HRV) as it is employed clinically as a biomarker for emotional state. It is also an independent predictor of many disease states – both cardiovascular and neurological diseases. We don't know why. Emotion regulation is associated with physiological arousal via the autonomic nervous system. Within the brain, tonic inhibition of the central amygdala (CeA) by the medial prefrontal cortex (mPFC) is critical for emotional regulation. Emotional dysregulation is associated with the development of mental illness and altered HRV. It remains unclear whether altered HRV is the cause or the consequence of the emotion dysregulation.

Project: This research project will aim to elucidate the pathways involved in the interaction between emotional centres and brainstem regions and their contribution to HR, HRV and behaviour modulation. We will use cutting-edge neuroscience methods to enable light-mediated control (optogenetics) of brain pathways between the amygdala and brainstem circuits regulating HR/HRV. This will involve stereotaxic brain injections of novel replication-deficient viruses and measurement of physiological function.

Expected outcome: This work will provide the foundation for understanding modulation of HR/HRV in the context of anxiety, panic and emotional dysregulation. As a consequence, the work will help to understand how the interaction between breathing and HR might affect mental health.

Project Supervisor:

Dr Mariana Melo

Project co-supervisor

Prof Andrew Allen

Project Availability:

- PhD
- Honours
- Master of Biomedical Science

Clark Group

Contact: Dr Mike Clark
Email: michael.clark@unimelb.edu.au
Location: Kenneth Myer Building
Website: go.unimelb.edu.au/ak9j

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.

Neuropsychiatric disorder 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. Hundreds of genes in our DNA have been identified that confer disease risk, however, we have a poor understanding of how changes in their expression and splicing confer disease risk. This project will utilize Nanopore sequencing, a ground-breaking technique, to decipher the expression and splicing patterns of neuropsychiatric risk genes in human brain and stem cell models of brain development. This will provide an unrivalled resource for discovering 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. The opportunity exists to perform the sequencing and/or conduct analysis of the expression data and this project would suit students interested in either laboratory work or computational analysis.

Project Supervisor:

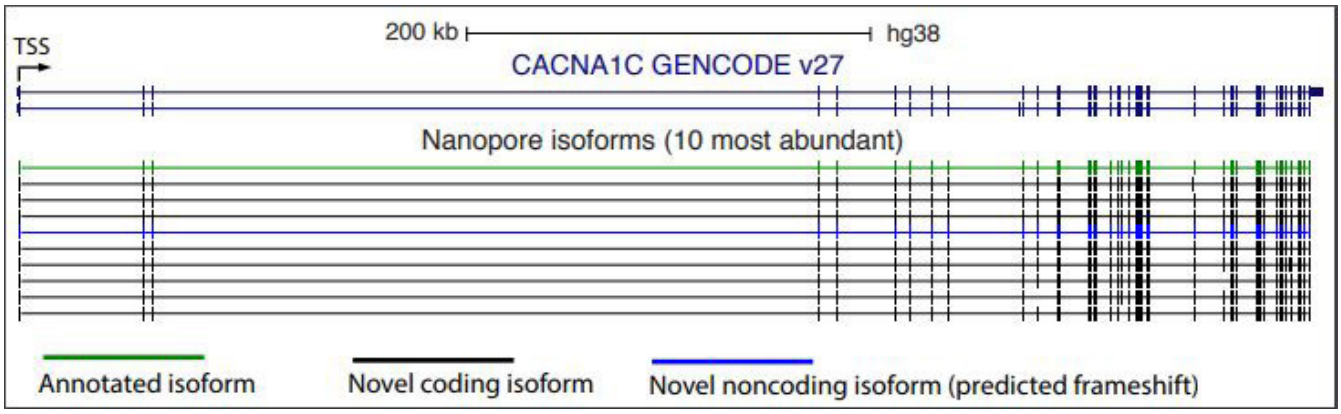
Dr Michael Clark

Project Co-supervisor:

Dr Ricardo de Paoli-Iseppi

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science



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

Project: Deciphering how our genes control 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 mRNA products (known as isoforms), but current technologies lack the ability to identify and functionally characterise the repertoire of gene isoforms controlling brain development. This project will profile gene isoforms in developing brain cells using long-read single cell RNA sequencing, a ground-breaking new technique for characterising isoform expression in individual cells, and determine their functional roles. We are using both in-vivo samples and differentiating stem-cells into cortical neurons and cerebral organoids, two cutting-edge models of human brain development. This project will 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 perform bioinformatic analysis of single-cell expression data and/or lab-based discovery of isoform functions and would suit students interested in either laboratory work or computational analysis.

Project Supervisor:

Dr Michael Clark

Project Availability:

- Honours
- Master of Biomedical Science

Project: How do our genes cause neuropsychiatric disorders?

Our genes play a key role in our risk for developing neuropsychiatric disorders such as schizophrenia, bipolar disorder and depression. However, while many risk genes have been discovered, we don't have a good understanding of what goes wrong with these genes or how they increase risk of disease. Our research has identified many new RNA products from neuropsychiatric risk genes, some of which may confer disease risk. This project will use a combination of cutting-edge technologies, (including Nanopore long-read sequencing, stem-cell models of disease, antisense oligonucleotides, mass spectrometry and bioinformatics) to investigate the function of these RNAs and their protein products and decipher how these genes cause risk for disease. This project will provide crucial new knowledge into the causes of neuropsychiatric disorders and potentially identify novel targets for future therapeutics. The opportunity exists to focus on the lab side and/or the bioinformatic aspects of this project and it would suit students interested in either laboratory work or computational analysis.

Primary Supervisor:

Dr Michael ClarkPrimary Co Supervisor

Dr Ricardo De Paoli-Iseppi

Project Availability:

- PhD
- Honours
- Master of Biomedical Science

Project: Coding the future: next-gen bioinformatic tools for nanopore data

Oxford Nanopore long-read sequencing is a cutting-edge approach with a number of unique features, including the real time sequencing of DNA or native RNA without the read length limits of traditional sequencing technologies. In addition, nanopore sequencing has extreme portability (take the sequencer to the sample) and can also detect nucleic acid base-modifications. This combination of unique attributes allows the use of nanopore sequencing in many novel (as well as existing) applications. Our lab has developed several new tools and applications for nanopore sequencing but there is much more that could be done to enable gene expression analysis, data visualisation, single cell sequencing and more. The opportunity exists for a student interested in bioinformatics or computational biology to develop new applications for nanopore sequencing to help address previously intractable biological questions.

Primary Supervisor:

Dr Michael Clark

Project Availability:

- PhD
- Honours
- Master of Biomedical Science

Project: Coding the future: next-gen bioinformatic tools for nanopore data

Oxford Nanopore sequencing is a cutting-edge technology for gene expression analysis with a number of unique features, including sequencing of native RNA, real time data output and long-reads with no length limit. In addition, nanopore sequencing can also detect epigenetic modifications of DNA and RNA. This combination of unique attributes allows the use of nanopore sequencing in many novel (as well as existing) applications. Our lab has developed new tools and applications for nanopore single-cell RNA-seq; RNA splicing analysis; and sequencing of native RNA, but there is much more that could be done to enable gene expression analysis, data visualisation, single cell sequencing and more. The opportunity exists for a student interested in bioinformatics or computational biology to develop new software tools and applications for nanopore sequencing to help address previously intractable biological questions.

Primary Supervisor:

Dr Michael Clark

Project Availability:

- PhD
- Honours
- Master of Biomedical Science

Project: How does the epitranscriptome control brain function?

Project Description: Regulation of gene expression is fundamental for the development and function of the human brain. Epigenetic modifications of RNAs, such as N6-methyladenosine (m6A), have been reported to function as critical regulators of gene expression, splicing and gene function. m6A is the most abundant RNA modification and m6A levels are highest in brain. We have been investigating m6A using nanopore direct RNA sequencing, which can simultaneously characterise the transcriptome and the epitranscriptome. This has identified unique epitranscriptomic profiles in each brain region and heavily modified RNAs of unknown function. This project will use a combination of innovative technologies, including direct RNA sequencing, to investigate the cell-type and sub-cellular localisation of modified RNAs and the functional roles of RNA modifications on coding genes and long-noncoding RNAs. This project will reveal new insights into brain region specificity and function, providing new avenues for investigation into neurological development and disease. The opportunity exists to perform lab-based discovery of m6A functions as well as bioinformatic analysis of direct RNA sequencing data and would suit students interested in either laboratory work and/or computational analysis.

Primary Supervisor:

Dr Michael Clark

Project Availability:

- PhD
- Honours
- Master of Biomedical Science

Furness Group

Contact: Prof John B Furness
Email: j.furness@unimelb.edu.au
Location: Department of Anatomy & Neuroscience.
Website: go.unimelb.edu.au/y65i

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 understnd digestive function and to treat bowel diseases through stem cell therapies, new bioactive compounds and neuromodulation.

Project: Neural control of intestinal inflammation – therapies for inflammatory bowel disease

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 Ruslan Pustovit

Project Co-supervisor:
Prof John B Furness

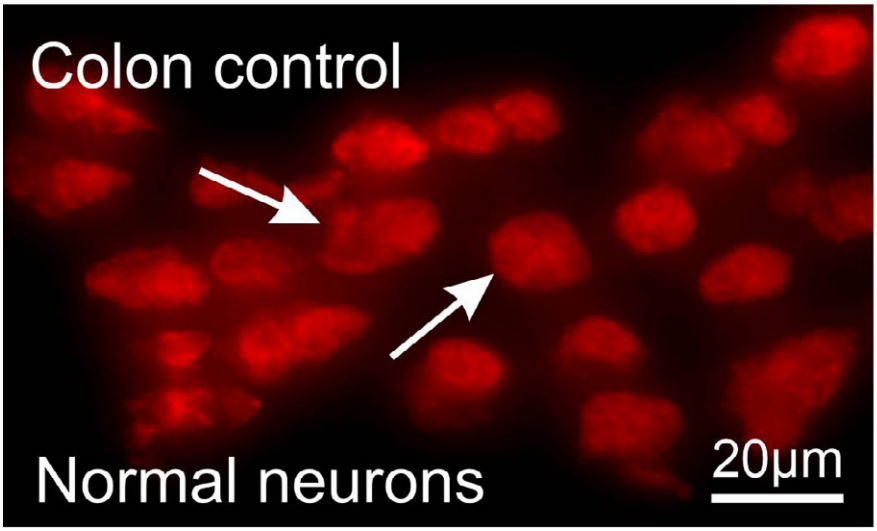
Project Availability:
- M.Phil/PhD
- Honours
- Master of Biomedical Science

Project: How the stomach and brain communicate

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

Prof John B Furness

Project Co-Supervisors

Dr. Martin Stebbing

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science

Project: A stem cell therapy for Hirschsprung Disease

Project Description: 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, fecal soiling, and associated psychosocial problems. Consequently, alternative treatments are needed.

In this project you will participate in our HSCR program, which includes the rescue of HSCR rats, the development of stem cell therapies and evaluation of recolonization of the enteric nervous system using structural and functional methods.

Primary Supervisor:

Prof John Furness

Project Availability:

- PhD
- Honours

Project: The INSL5/ relaxin (RXFP4) receptor axis: How the large intestine is controlled

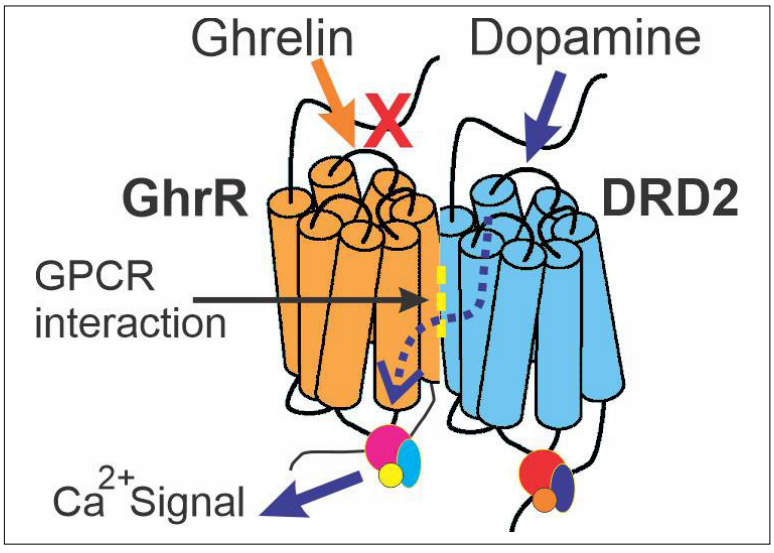
Project Description: Our team has been investigating structurally-related analogues and the physiological roles of the gut hormone, insulin-like peptide 5 (INSL5), an endogenous ligand for the G protein-coupled receptor RXFP4. Our recent discoveries indicate that INSL5 is a physiological regulator of colonic emptying and that RXFP4 agonists and antagonists have the potential for treating constipation and diarrhea, respectively, unmet medical needs that are associated with significantly reduced health-related quality of life.

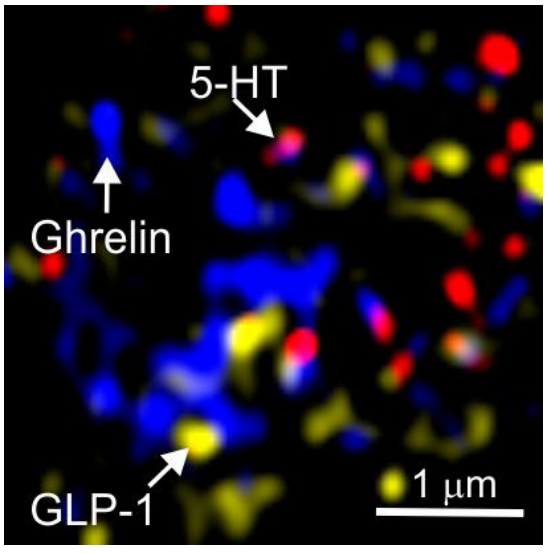
Primary Supervisor:

Dr Sarah Gordon

Project Availability:

- PhD
- Honours
- Master of Biomedical Science





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

Gunnersen Group

Contact: Dr Jenny Gunnersen
Email: jenny.gunnersen@unimelb.edu.au
Location: Department of Anatomy and Physiology

Our broad research goal is to understand how neurons become connected into functional circuits. We investigate how synapses, the connections between neurons, form during brain development and how they are affected in neurological disorders.

Plasticity, the formation of new synapses and strengthening of existing synaptic connections (as well as synapse weakening and loss) is vital for learning and memory in the healthy brain. On the other hand, abnormal synapse numbers and activity are seen in 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

Project Availability:
- Honours
- Master of Biomedical Science
- PhD

Project: How does Sez6 promote excitatory synapse development and maintenance?

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

Project Availability:
- Honours
- Master of Biomedical Science
- PhD

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

Project Availability:
- Honours
- Master of Biomedical Science
- PhD

Keast-Osborne Group

Contact: Prof Janet Keast and Dr Peregrine Osborne (co-lab heads)
Email: jkeast@unimelb.edu.au and peregrine.osborne@unimelb.edu.au
Location: Department of Anatomy and Physiology

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.

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 different in males and females and continue to be 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 are determined correctly. Very little is known about how this part of the autonomic nervous system develops and what initiates its sexual dimorphism. Understanding this initial spinal cord connectivity 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 the developing arterial, venous and lymphatic systems in the bladder and urethra.

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

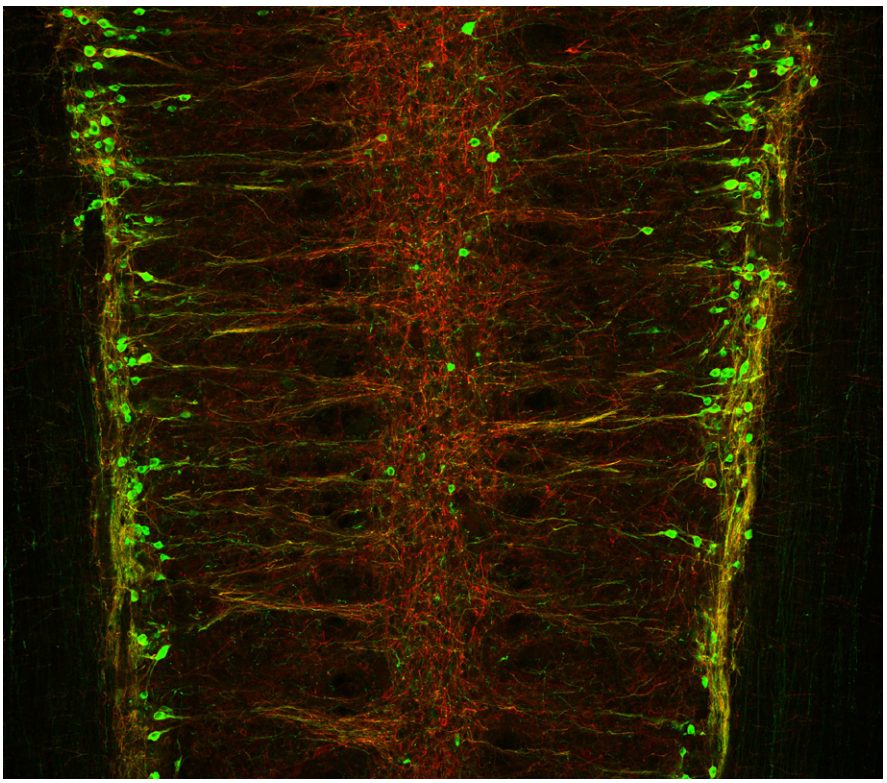
A range of studies are available in this area and are especially suited to students with a strong background in neuroanatomy, neurophysiology or bioengineering. Development of devices to control urogenital function first needs a high-resolution map of neuronal connections with each tissue and region 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

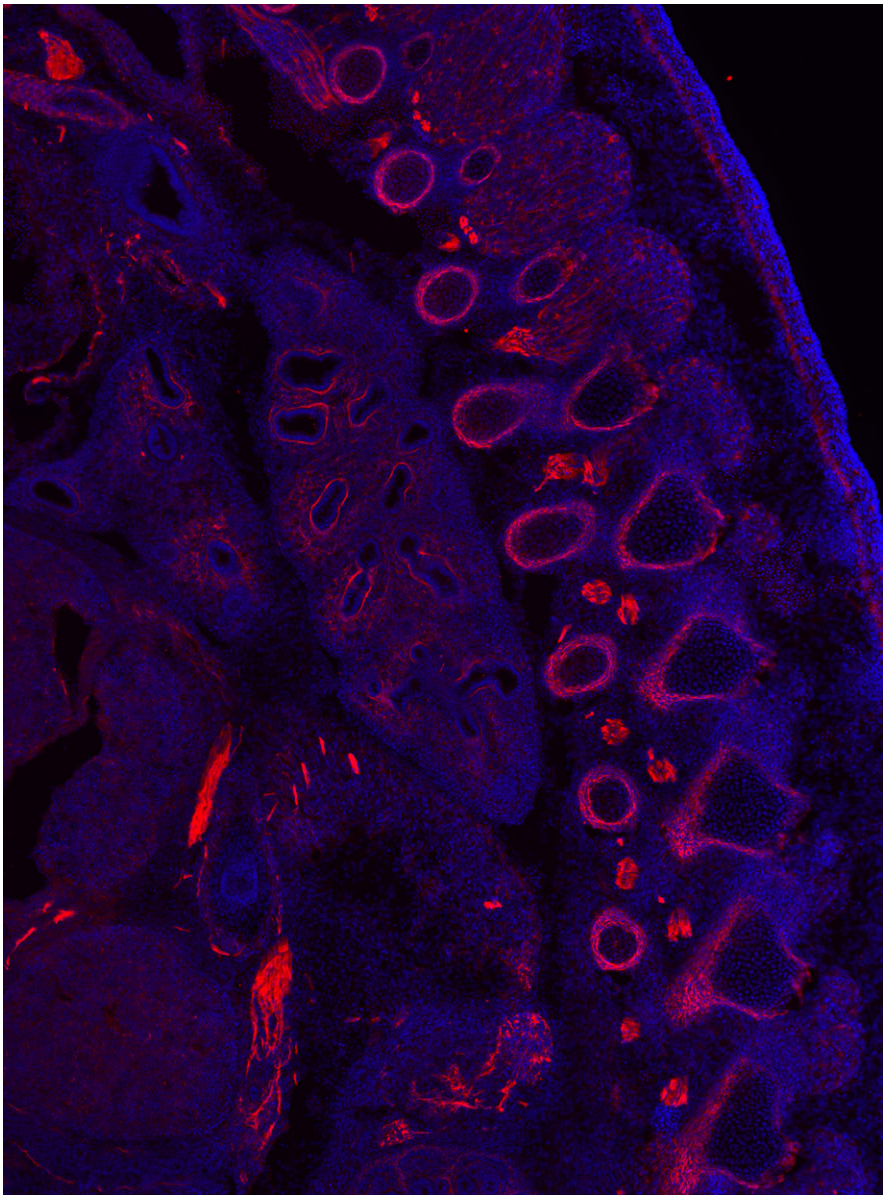
Project Co-supervisor:
Dr Peregrine Osborne

Project Availability:
- M.Phil/PhD
- Honours
- Master of Biomedical Science



Project: Development of vascular and autonomic nerve networks

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

Project Co-supervisor:

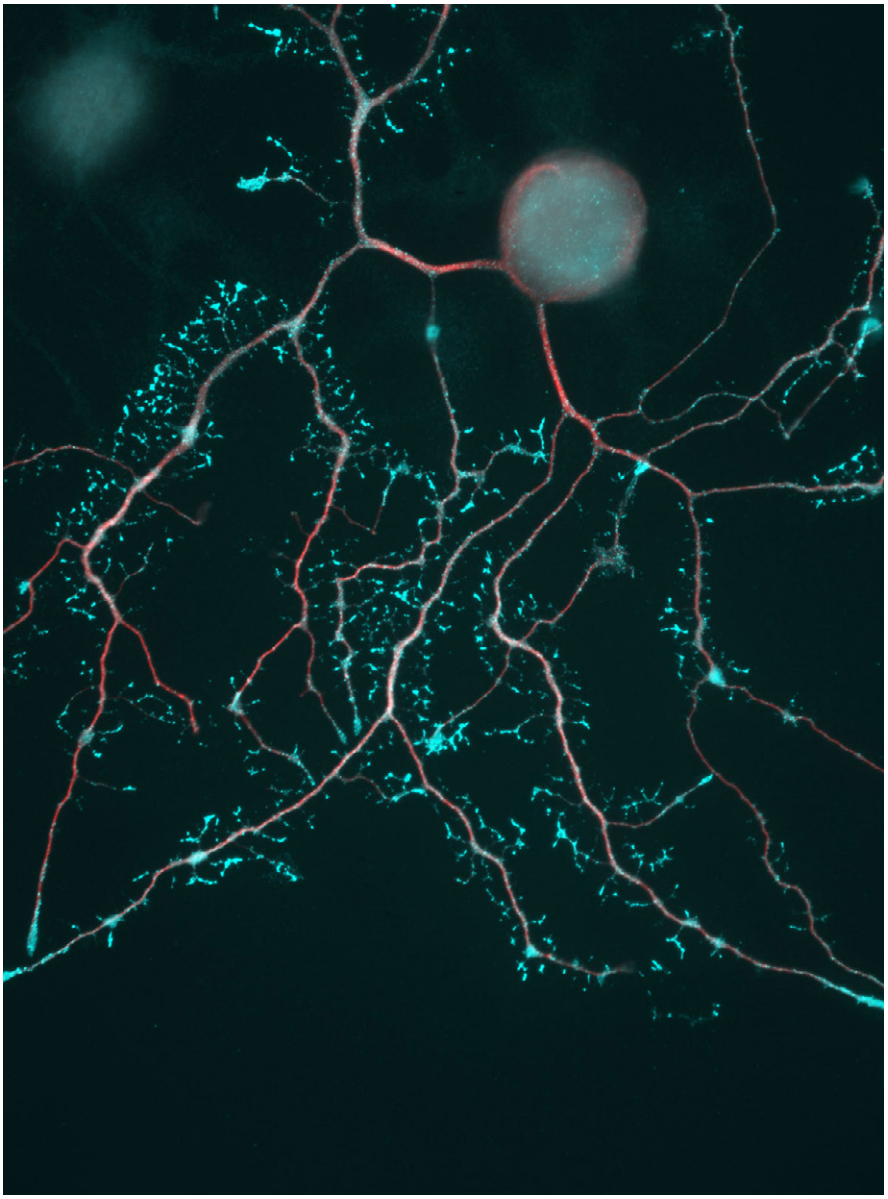
Dr Peregrine Osborne

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science

Project: 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

Project Co-supervisor:

Dr Peregrine Osborne

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science

Murray Group

Contact: A/Prof Simon Murray
Email: ssmurray@unimelb.edu.au
Location: Department of Anatomy and Physiology

Human demyelinating diseases, such as multiple sclerosis (MS), have a devastating impact on quality of life. The Myelin Biology Lab investigates the development and repair of myelin - the insulating sheath wrapping around many axons in the peripheral (PNS) and central nervous systems (CNS). We use mice as a model system to study how myelin develops and is repaired after brain injury. Current projects utilise cellular and mouse models and focus on the signalling and transcriptional mechanisms that control myelination, and in optimising strategies to promote myelin repair.

Project: Can mimetics of BDNF promote remyelination after injury?

In CNS demyelinating diseases, oligodendrocytes (the cells that generate myelin) progressively die. However, they possess an innate capacity to regenerate themselves and repair the lost myelin. Unfortunately, over time and repeated demyelinating events, this capacity for regeneration and repair reduces. We have identified that BDNF plays an important role in myelin development and repair. Building on these findings, we have developed novel low molecular weight peptides designed to selectively mimic the agonist properties of BDNF. This project is multifaceted in that it aims to use in vitro assays to optimise and characterise novel next-generation peptides, and use in vivo assays to investigate whether these novel BDNF mimetic peptides can promote myelin repair using animal models of nervous system demyelination.

Project Supervisor:

A/Prof Simon Murray

Project Availability

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

Project: Analysis of myelin specific transcription factors

The myelin sheath - a multi-layer membrane that wraps around many nerves in the central nervous system (CNS) - is critical for optimal brain function. Myelin sheaths are made by cells called oligodendrocytes and most myelin sheaths are formed in early postnatal development, but new sheaths can be added throughout life either after brain injury or in response to learning. However, the molecular mechanisms that regulate these dynamic changes in myelin sheath growth have not been identified. The overall aim of this project is to identify and characterise novel molecular mechanisms that control myelin sheath growth in the CNS. We will use innovative interdisciplinary methods to identify novel signalling pathways and protein interactions that control oligodendrocyte development and function.

Project Supervisor:

A/Prof Simon Murray

Project Availability

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

Stamp & Hao Group

Contact: Dr Lincon Stamp and Dr Marlene Hao
Email: lstamp@unimelb.edu.au; hao.m@unimelb.edu.au
Location: Department of Anatomy and Physiology

Proper development and function of the digestive tract is crucial for good health. Gut function relies on the co-ordinated activity of neural circuits in the enteric nervous system, a network of neurons and glia located within the wall of the gastrointestinal tract. Our lab focuses on investigating the plasticity of the enteric nervous system and the development of stem cell therapy to treat digestive diseases.

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 this 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

Project Availability:

- M.Phil/PhD
- Master of Biomedical Science

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

Project Availability:

- M.Phil/PhD
- Master of Biomedical Science

Project: Circadian plasticity of the enteric nervous system

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. In this project, we will examine how plasticity of communication between enteric neurons leads to changes in gut function using live calcium imaging to record neuronal activity. We will also investigate how nutrient detection changes through the circadian cycle, and how these forms of plasticity decline during ageing.

Project Supervisor:

Dr. Marlene Hao

Project Co-supervisor:

Dr. Lincon Stamp

Project Availability:

- M.Phil/PhD
- Master of Biomedical Science

Project: A gut feeling about new therapies for brain cancer treatment

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 neural stem cells in the brain. Glial cells are a prominent part of the enteric nervous system, but gliomas in the gut are very rare and are generally benign. How are enteric glial cells protected against developing aggressive tumours? In this project, we will use a novel line of transgenic mice to investigate enteric glial cell proliferation and their interactions with immune cells in the gut.

Project Supervisor:

Dr Marlene Hao

Project Co-supervisor:

Dr Lincon Stamp

Project Availability:

- M.Phil/PhD
- Master of Biomedical Science

Project: Gene expression analysis of enteric glia in health and disease

Enteric glial cells are a crucial population of cells in the gastrointestinal tract. They play many important roles in the support of enteric neurons. In addition, they act as the neural stem cells of the gut, which is a unique property of enteric glia that is not found in other glial populations elsewhere in the nervous system. In this project, we will investigate how gene expression patterns in enteric glia differ from that of other glial cells including astrocytes and oligodendrocytes of the central nervous system. In addition, we will investigate how gene expression patterns change in enteric glia in a model of cancer.

Project Supervisor:

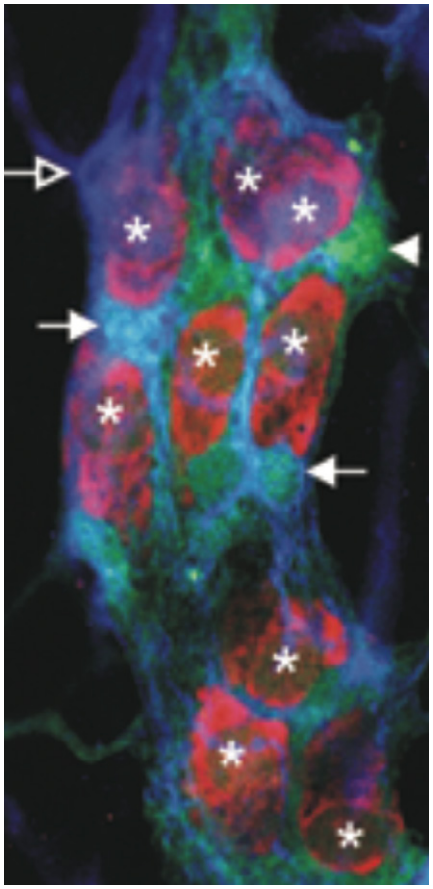
Dr. Marlene Hao

Project Co-supervisor:

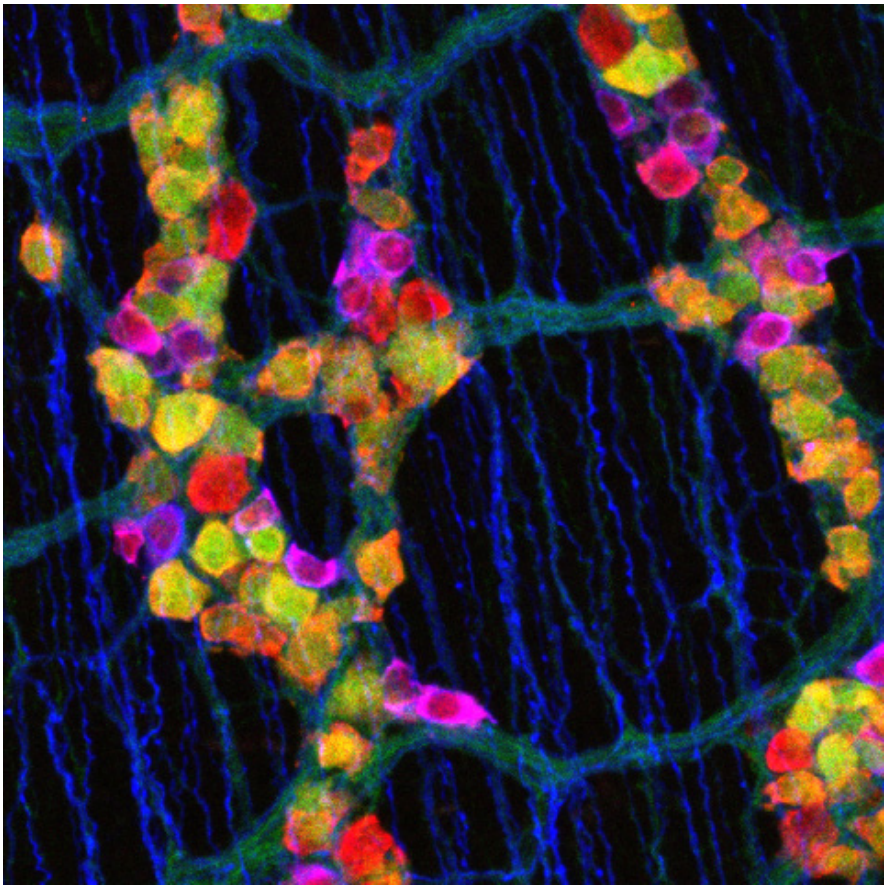
Prof Christine Wells
Dr Jarny Choi
Dr Lincon Stamp

Project Availability:

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



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



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.

Yao Group

Contact: Dr Song Yao
Email: song.yao@florey.edu.au
Location: Department of Anatomy and Physiology

The Yao Laboratory is located in the Department of Anatomy and Physiology. The laboratory's main interest is to understand how the brain controls the cardiovascular system and how these mechanisms become dysfunctional in diseases such as heart failure and hypertension. Recently, we have explored mechanisms whereby inflammation can cause increased activity in certain brain areas which ultimately causes an increase in sympathetic nerve activity and blood pressure. Our laboratory is particularly interested in how inflammation and inflammatory mediators might lead to increases in blood pressure in hypertension. We use a range of techniques in the laboratory. These include, neuropharmacology, electrophysiology, radiotelemetry, immunohistochemistry, confocal microscopy.

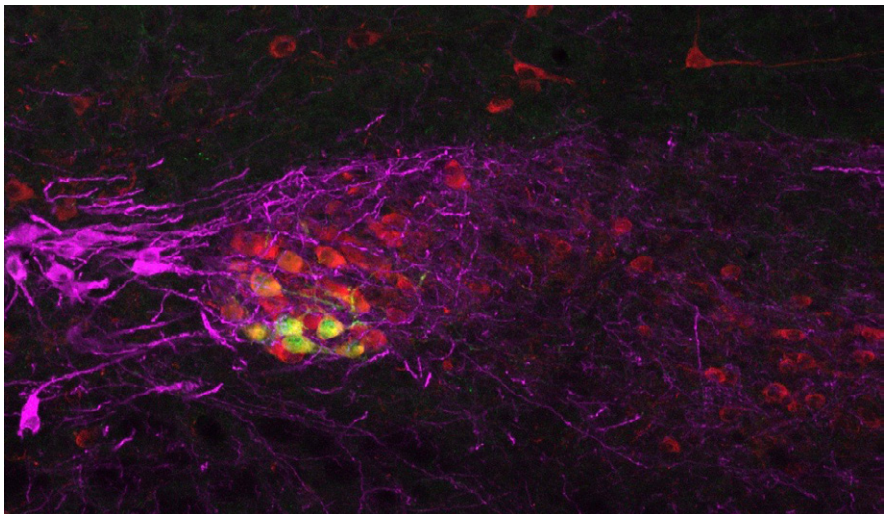
Project:Neuroinflammation: Impact of diabetes on microglia morphology in cardiovascular control centres

There is a link between diabetes and cardiovascular disease, the latter being the most prevalent cause of morbidity and mortality in diabetic patients. For example, hypertension is very common in patients with both type 1 and type 2 diabetes with prevalence rates of 30% and 60% respectively1. There is good evidence to suggest that there are changes in the brain centres that control cardiovascular function in pre-clinical animal models of diabetes such that there is impaired regulation of cardiovascular neurons in streptozotocin (STZ)-treated rats2. This project will investigate changes in microglia morphology in critical brain circuits that control cardiovascular function in mice with STZ-induced diabetes.

Project Supervisor:
Dr Song Yao

Project Co-supervisor:
Dr William Korim

Project Availability:
- Honours



Project: Central cardiovascular control: Role of inflammatory cytokines and neuroinflammation in hypertension

There is much evidence to suggest that inflammatory cytokines are increase in a number of cardiovascular diseases such as hypertension and heart failure. However, the effects of these cytokines in brain nuclei critical for blood pressure control is currently not well known. This project will investigate the effects of inflammatory cytokines on blood pressure, heart rate and sympathetic nerve activity when exogenously applied to the central nervous system. The successful candidate will be exposed to a wide range of techniques including small animal surgery, in vivo physiology, immunohistochemistry and microscopy.

Project Supervisor:
Dr Song Yao

Project Co-supervisor:
Dr William Korim

Project Availability:
- Honours
- PhD
- Masters of Biomedical Science

Stem Cell and Developmental Biology

Hime Group

Contact: Prof Gary Hime
Email: g.hime@unimelb.edu.au
Location: Department of Anatomy and Physiology
Website: go.unimelb.edu.au/g65i
go.unimelb.edu.au/965i

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: 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:

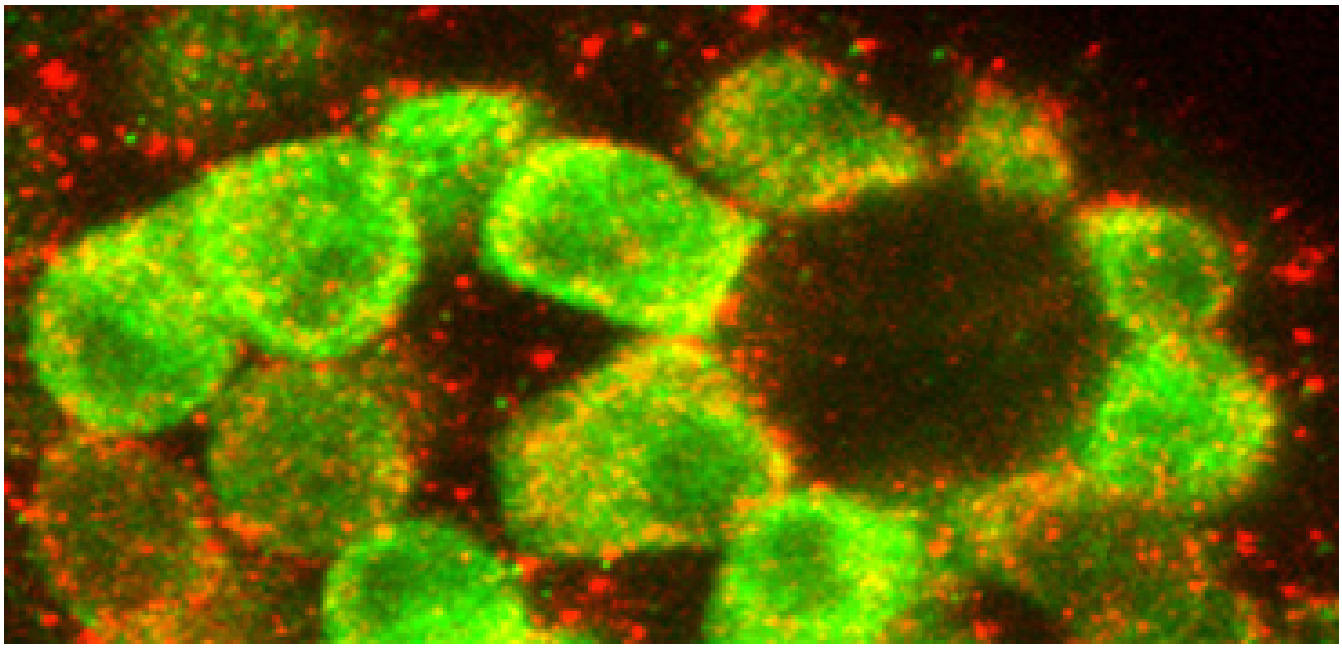
Prof Gary Hime

Project Co-supervisor:

Dr Nicole Siddall

Project Availability:

- M.Phil/PhD
- 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

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science

Project: Regulating male fertility: identifying new regulators of gamete formation

Production of spermatozoa is a highly regulated process that involes genes interacting with environmental signals to produce spermatozoa from a population of germline stem cells. This project will use a variety of genetic techniques (RNA interference, CRISPR, mutant analysis) with advanced microscopy and cellular analysis to identify new regulators of this process. We work with groups studying human infertility to identify genes that affect human male infertility and as these genes are often involved in other disease processes they provide warnings for overall human health.

Primary Supervisor:

Prof Gary Hime

Co-Supervisor:

Dr Nicole Siddal

Project: Regulating male fertility: identifying new regulators of gamete formation

Production of spermatozoa is a highly regulated process that involes genes interacting with environmental signals to produce spermatozoa from a population of germline stem cells. This project will use a variety of genetic techniques (RNA interference, CRISPR, mutant analysis) with advanced microscopy and cellular analysis to identify new regulators of this process. We work with groups studying human infertility to identify genes that affect human male infertility and as these genes are often involved in other disease processes they provide warnings for overall human health.

Project Supervisor:

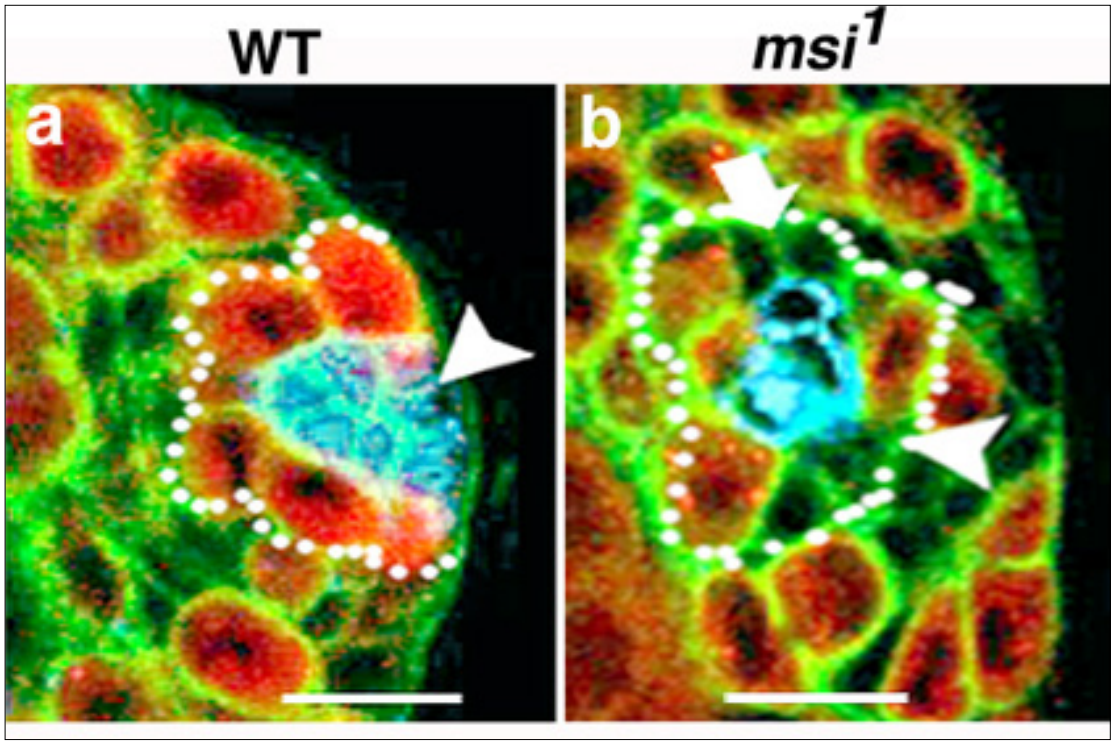
Prof Gary Hime

Project Co-supervisor:

Dr Nicole Siddall

PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science
- Honours



PROJECT: **AMITOSIS: UNDERSTANDING HOW CELLS CAN DIVIDE WITHOUT UNDERGOING MITOSIS**

We have identified that during Drosophila salivary gland development an increase in cell number occurs without mitotic activity. This is an unusual form of cell division that is specific to polyploid cells, and occurs in greater than 30% of human tumours. We will use Drosophila genetics to discover how this process is regulated and potentially identify new ways of treating tumour growth.

Project Supervisor:

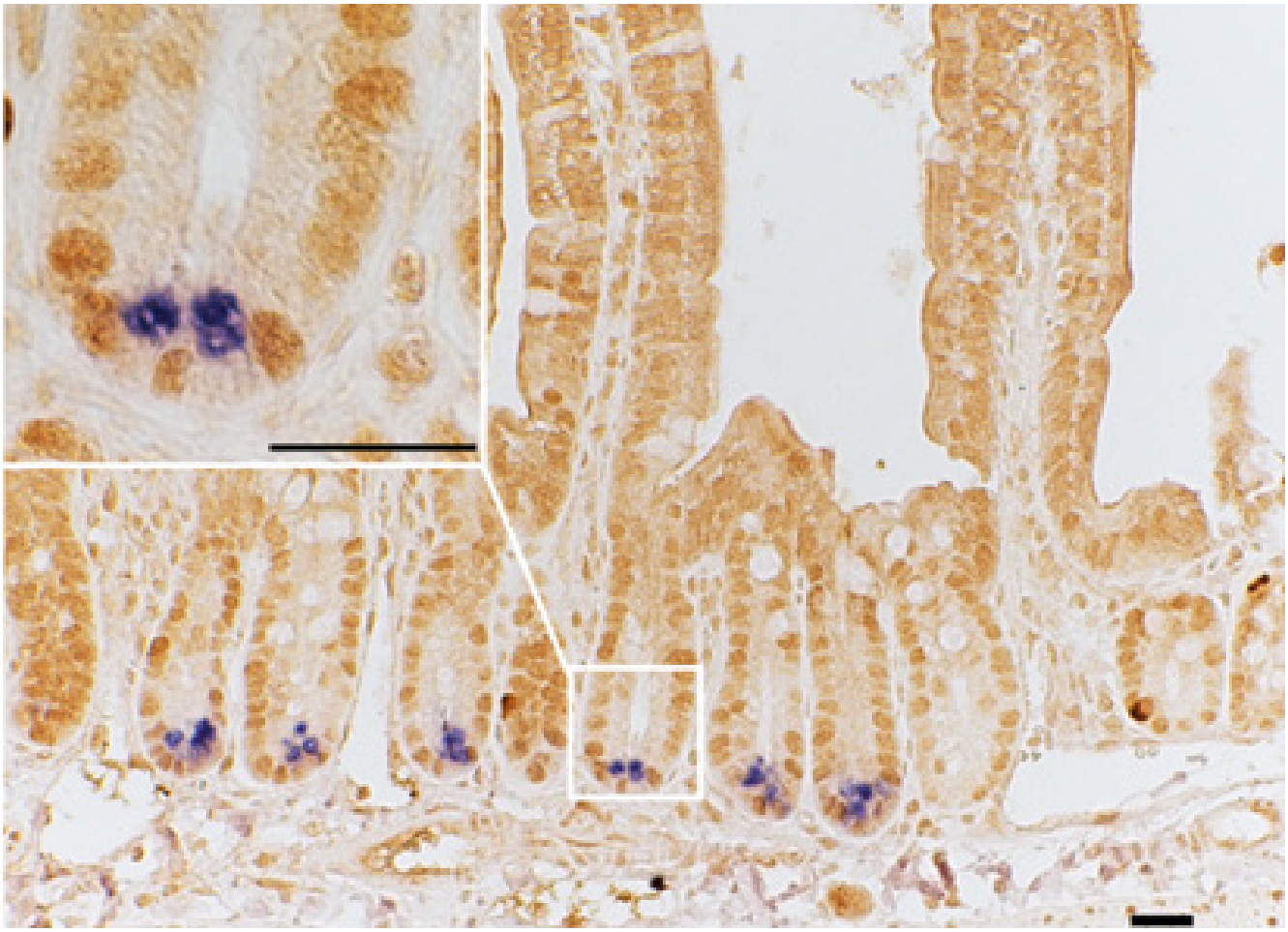
Prof Gary Hime

Project Co-supervisor:

Dr Nicole Siddall

PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science



Porello Group

Contact: A/Prof Enzo Porello
Email: enzo.porrello@unimelb.edu.au
Location: Murdoch Children's Research Institute
Website: go.unimelb.edu.au/p7hr
mcri.edu.au/heartregeneration
go.unimelb.edu.au/47hr

Frontline therapies for childhood heart disease have not changed in over 30 years. Our vision is to transform the treatment of childhood heart disease using stem cell technologies. Our laboratory harnesses the power of pluripotent stem cells to create human models of human disease as a platform for therapeutic development. Our laboratory employs a range of cutting edge technologies including patient-derived induced pluripotent stem cells (iPSCs), genome editing (CRISPR/Cas9), genomic sequencing, transcriptomics (including single cell RNA-seq) and animal models to identify new drug targets for heart regeneration.

Project: Disease modelling of inherited cardiomyopathy using pluripotent stem cell models

Inherited cardiomyopathies are associated with an abnormal structure of the heart and a reduction in functional capacity. The two most common forms of inherited cardiomyopathies are hypertrophic (HCM) and dilated cardiomyopathy (DCM). While many of the causal genes that lead to HCM and DCM have been identified, the impact of specific variants on disease progression is less clear. Our lab work with human induced pluripotent stem cells (hiPSC) that we differentiate into heart cells (cardiomyocytes). Using this innovative approach, in combination with CRISPR/Cas9 gene editing, this project aims to evaluate the putative disease-causing properties of a new variant in stem cell-derived cardiac cells and organoids. This project encompasses pluripotent stem cell culture, cardiac differentiation, and disease phenotyping by high-content imaging. The outcome of this project will be the characterization of novel gene variants in cardiac disease pathogenesis.

Primary Supervisor:

Prof Enzo Porello

Project Co-Supervisor

A/ Prof David Elliot
Dr Rosie Hyslop
Dr Kevin Watt

Project Availability:

- PhD
- Master of Biomedical Science

Project: Identification of novel mechanisms of anthracycline-induced cardiotoxicity

Anthracyclines are the front-line therapy for many paediatric cancers. While these drugs are highly effective chemotherapeutics, their clinical usage is limited by significant dose-dependent and irreversible cardiac damage in many patients. Various mechanisms of anthracycline-induced cardiotoxicity have been reported. Yet, how anthracyclines cause cardiotoxicity remains unclear. Using human pluripotent stem-cell derived heart cells (cardiomyocytes), we have developed an approach to model anthracycline-induced cardiotoxicity in vitro. In this project, we will use advanced proteomic techniques to identify novel binding targets of the anthracycline in cardiomyocytes. The importance of these targets will be interrogated using imaging and biochemical techniques. This research may provide a basis for the development of novel therapies that protect the heart from cardiotoxicity.

Primary Supervisor:

Prof Enzo Porello

Project Co-Supervisor

A/ Prof David Elliot
Dr James McNamara

Project Availability:

- PhD
- Master of Biomedical Science

Project: Biomechanical signalling in human heart failure

Heart failure is associated with tissue remodelling that alters biomechanical force and intracellular signalling. The relationship between these biophysical and biochemical changes and their contribution to heart function during heart failure remains unclear. To address this knowledge gap, this project will utilise an extensive collection of human cardiac tissue samples and induced pluripotent stem cell (iPSC) lines available through the Melbourne Children's Heart Tissue Bank. The project's primary objective is to explore the biomechanical defects that underlie heart failure using cardiac physiology. Integration of these physiological findings with state-of-the-art mass spectrometry techniques to analyse biochemical changes in heart tissue will establish a comprehensive map of the signaling events responsible for mechanical dysfunction during human heart disease. Ultimately, this research aims to identify potential new therapeutic targets for the treatment of heart failure.

Primary Supervisor:

Prof Enzo Porello

Project Co-Supervisor

A/ Prof David Elliot
Dr Kevin Watt

PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science

Project: Regenerating the heart: new approaches to treat heart failure

Heart failure affects more than 26 million people worldwide and remains a leading cause of death globally. Heart failure can arise because of inherited or acquired conditions. During heart failure, the cells of the heart (cardiomyocytes) die contributing to further declines in functional capacity. Since the adult heart is the least regenerative organ in the human body, the loss of cardiomyocytes is irreversible. A lack of targeted therapies to promote heart regeneration means that transplantation remains essential for many patients. In this project, we will characterise new candidate compounds to promote heart regeneration in genetic forms of cardiomyopathy. The student will use human induced pluripotent stem cell (hiPSC) cultures and mouse models to test the regenerative potential of candidate compounds. The student will characterise the biochemical and functional effects of compounds using molecular biology techniques (imaging, flow cytometry, RNA sequencing) and physiological measures (echocardiography and electrocardiography). The outcomes of this work will support efforts to find new therapies to treat genetic forms of cardiomyopathy.

Primary Supervisor:

Dr Thibault Renoir

Project Co-Supervisor

Prof Tony Hannan

Smith Group

Contact: A/Prof Kelly Smith
Email: kelly.smith1@unimelb.edu.au
Location: Department of Anatomy and Physiology

The Smith group is focussed on identifying the genetic and cellular regulators of heart development; in otherwords: how do we build a heart?

The heart develops by differentiating cells and organising them in a stereotypical pattern to build this organ. The fact that this structure is more or less identical between individuals demonstrates that a tightly controlled genetic program instructs this process. The lab is interested in identifying such genes, determining how they function, and uncovering the cellular processes they regulate. We use the zebrafish model for much of our discovery-based projects. The zebrafish is an excellent genetic model and the transparency of the embryos and availability of fluorescent transgenic reporter lines permits live imaging of organogenesis. For some projects, we translate our discoveries to mouse models to investigate evolutionary conservation. The long-term objective of the lab is to contribute to our knowledge of how to build a heart, gathering along the way information that will assist bioengineering efforts and help with diagnosis and treatment of genetic-based heart disease.

Project: Identifying the role novel proteins have on implantation and placentation: implications for pregnancy complications.

Project Description: Up to 15% of pregnancies develop complications due to poor embryo implantation or defective placental development. These early steps are essential for a healthy and successful pregnancy. Implantation involves the outer wall of the fertilised embryo (termed trophoblast) embedding into the uterine wall, invading the maternal tissue, and establishing the placenta: an integrated and highly vascularised interface for nutrient and waste exchange. If trophoblasts are too invasive, the placenta embeds too deeply, which can result in severe haemorrhage and is a significant contributor to maternal death. At the opposite extreme, insufficient trophoblast invasion can result in a placenta that is too shallow, which is associated with a spectrum of pregnancy complications including preterm birth, preeclampsia, and foetal growth restriction. The developmental problems that stem from a complicated pregnancy have lifelong consequences of significant emotional, medical, and economic burden. Understanding the process of implantation and impaired placental development is necessary for the development of preventative measures and is of significant clinical need. This project will investigate mouse models with abnormal implantation and placental development. It will determine how and why disease occurs and investigate potential therapeutic interventions.

Primary Supervisor:
Dr Marlene Hao

Project Co-Supervisor
Dr Lincon Stamp

Project Availability:

- PhD
- Honours
- Master of Biomedical Science

Project: Investigating left-right patterning of the heart

The heart is an asymmetric organ. Not only is it positioned on the left side of the body but it possesses asymmetry intrinsic to the organ itself. The heart begins as a simple symmetrical tube and asymmetry is imposed as the heart twists and bends to form what is called the "looped heart". This asymmetric morphogenesis always occurs with left-right bias in the same direction and is, therefore, not a random occurrence but genetically hardwired. The lab has identified an early left-right asymmetry that precedes asymmetric looping of the heart and we believe is instructive to directional cardiac looping – i.e. how the overall shape on an organ is made. We have developed a number of transgenic models to perform detailed imaging on live zebrafish embryos and we have developed genetic and chemical tools to study how this process is perturbed and what the consequences are to organ development. Methods used in the project will include embryology (of zebrafish), drug and chemical treatments, genetic crosses, molecular techniques (such as DNA extraction, PCR, gel electrophoresis), phenotypic screening by bright-field and fluorescence microscopy, confocal microscopy, image analysis and data quantification.

Project Supervisor:

A/Prof Kelly Smith

Project Availability:

- PhD
- Master of Biomedical Science
- Honours

Project: Mammalian coronary vascular development and its interaction with the extracellular matrix

The heart is a large and highly metabolic organ that requires its own blood supply to continue to respire and function. The coronary vasculature is a specialised network of blood vessels that carries oxygenated and deoxygenated blood to and from the heart. Cardiac arrest or myocardial infarction occurs due to occlusions of the coronary vasculature. It is the leading cause of death in the western world, providing a testament to how important this vascular network is. Blood vessels grow via sprouting angiogenesis, invading tissues that need a blood supply. This growth is dependent on growth factor signalling and growth factor signalling involves modification of the extracellular matrix. As the name suggests, the extracellular matrix (or ECM) exists outside the cell and is often described as a scaffold or network for cell-cell communication and for cells to adhere to. The ECM is composed of many different components, one of which is Hyaluronic Acid. We have identified a new enzyme that degrades Hyaluronic Acid and have shown an early role in embryonic angiogenesis in the trunk of the zebrafish embryo. We hypothesise this enzyme is essential for coronary vascular formation and have generate a mouse model to study this. The project will involve the analysis of mouse embryonic hearts to determine how the coronary vasculature is developing under normal and conditions of disturbed Hyaluronic Acid turn-over.

Project Supervisor:

A/Prof Kelly Smith

Project Availability:

- PhD
- Master of Biomedical Science
- Honours

Project: Formation of the trabecular layer during cardiac development

Trabeculae are ridges or protrusions that grow into the lumen of the heart, helping to make it more efficient. Defects in trabeculation cause cardiomyopathy (weakened heart muscle) and can result in heart failure. Excitingly, the lab has identifiied a genetic marker that labels trabeculae BEFORE they develop; in other words a “fate marker” or “lineage marker”. In addition, we have zebrafish mutant lines with defects in trabecular development. Using these mutants, combined with our novel fate marker, the project will investigate the genetic regulation of trabecular development and determine when things go wrong in these mutants.

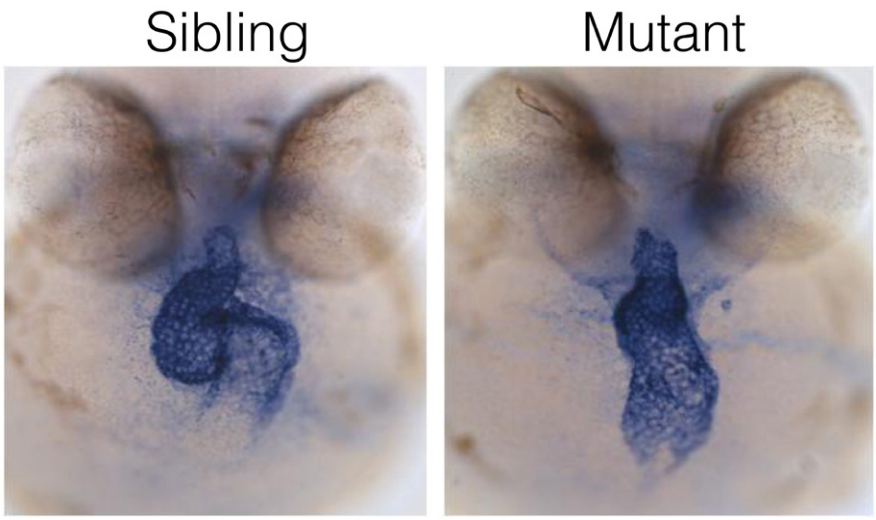
Methods used in the project will include embryology (of zebrafish), microinjection techniques, drug and chemical treatments, genetic crosses, molecular techniques (such as DNA extraction, PCR, gel electrophoresis, RNA synthesis), phenotypic screening by bright-field and fluorescence microscopy, confocal microscopy, image analysis, development of 3-dimensional renders of the heart, and statistical analysis.

Project Supervisor:
A/Prof Kelly Smith

Project Co-supervisor:
Dr Jessica Briffa
Dr Victoria Garside

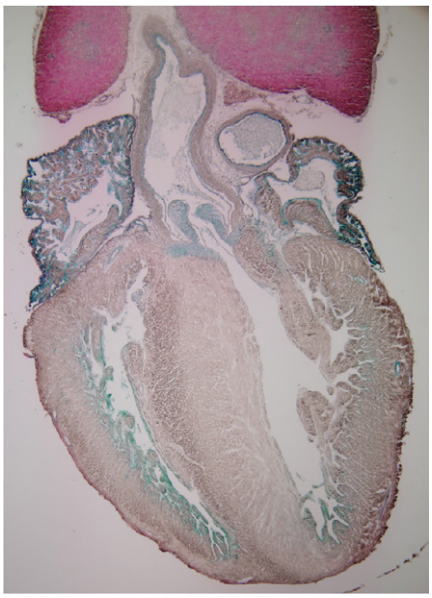
Project Availability:

- PhD
- Master of Biomedical Science
- Honours



In situ hybridisation stain outlining the heart and showing a looped wildtype heart (sibling) and an unlooped (mutant) heart

Project 2



1 day old mouse heart, LacZ-stained for the expression of an enzyme that degrades the extracellular matrix

Project 3

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:

Prof Christine Wells

Project Co-supervisor:

Dr Jarny Choi

Project Availability:

- M.Phil/PhD
- 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:

Prof Christine Wells

Project Availability:

- Honours
- Master of Biomedical Science

Project: A stem cell commons

This project aims to develop a new public health resource for stem cell researchers in Australia. The project will create a prototype of Australia's first stem cell registry. The student will draw on models that have been developed internationally as a framework for the project, but will also examine who might use a registry, how, and what features are needed by the Australian community for an effective resource. The student will participate in an MRFF-funded project and learn methods drawn from the public health, law and humanities sectors.

Project Supervisor:

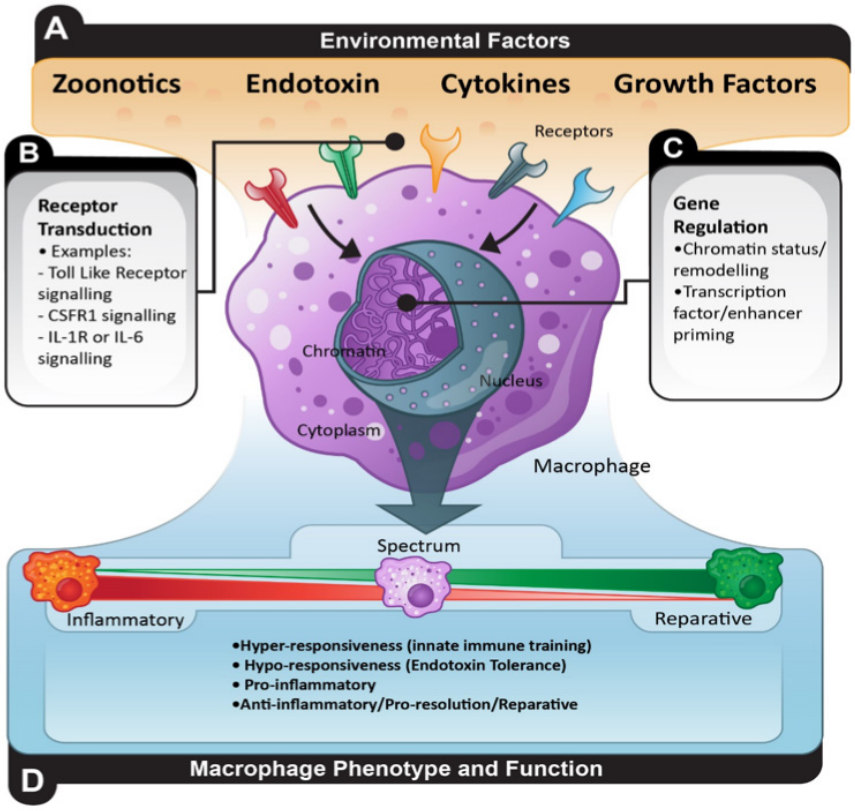
Prof Christine Wells

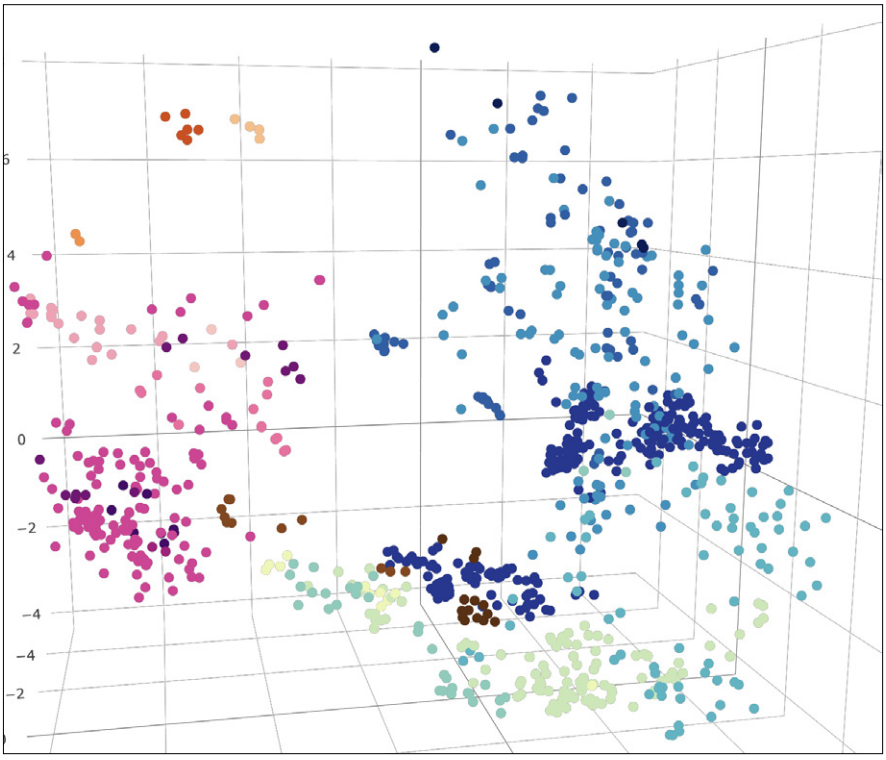
Project Co-supervisor

Prof Megan Munsie

Project availability

- PhD
- Master of Biomedical Science





Wilhelm Group

Contact: A/Prof Dagmar Wilhelm
Email: dagmar.wilhelm@unimelb.edu.au
Location: Department of Anatomy and Physiology
Weblink: go.unimelb.edu.au/7x5i

We study mechanisms of gene regulation that drive sex determination and the development of gonads using mouse as a model system to identify and understand the underlying cause of differences of sex development and infertility in humans.

Project: The role of ATP6AP2 in male and female fertility.

We have shown that loss of the gene Atp6ap2 in mouse somatic cells of the gonads, testes and ovaries, results in both male and female infertility. Recent research showed that this factor plays multiple roles in different cellular pathways. Using mouse as model system, this project characterizes its role in fertility and will therefore uncover critical mechanisms underlying testicular and ovarian development and disease.

Project Supervisor:

A/Prof Dagmar Wilhelm

Project co-supervisor

Dr Daniel Bird

Project availability

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

Project: The role of ATP6AP2 in adrenal cortex development

We developed a novel mouse model that is lacking the gene Atp6ap2 in the adrenal cortex. The characterisation of these mice will provide new insides into the development of the important organ and identify mechanisms when things go wrong. Adrenal glands produce hormones that help regulate your metabolism, immune system, blood pressure, response to stress and other essential functions. Abnormalities in development affect their function and causes diseases such as Addison's disease.

Project Supervisor:

A/Prof Dagmar Wilhelm

Project co-supervisor

Dr Daniel Bird

Project availability

- Honours
- Master of Biomedical Science

Melbourne Academy of Surgical Anatomy

Fogg Group

Contact: A/Prof Quentin Fogg
Email: quentin.fogg@unimelb.edu.au
Location: Department of Anatomy and Physiology

The Fogg Lab specialises in clinical anatomy that spans numerous areas of research and teaching. The Lab utilises numerous techniques, including dissection, 3D digitisation, medical imaging and histology. The main anatomical areas of interest are human limbs, and particularly their distal regions (hands and feet), although the Lab regularly applies its suite of techniques to other areas of the body. The main objective is to provide anatomical answers to clinical problems, so the Lab collaborates with clinicians nationally and internationally. We aim to improve patient outcomes by providing the clearest anatomical evidence base possible.

Clinical anatomy of the upper limb

The Fogg Lab looks at a wide range of anatomical features and relations, all from a clinical/surgical perspective. These projects utilise a diverse suite of techniques that include advanced dissection, 3D modelling, macrosectioning, and medical imaging (Xray, CT, MR, uCT) and a range of photographic and other visualisation protocols. We aim to provide comprehensive anatomical answers to clinically impactful questions. This project will build upon existing upper limb projects that interrogate regions such as the wrist, thumb, finger, shoulder and elbow. The specific region is subject to Donor availability and arranged in concert with the supervisors and student. These areas suffer from the same lack of reproducible anatomical data, and a level of detail suitable for the demands of modern clinical managament of injuries.

Project Supervisor:
A/Prof Quentin Fogg

Project Availability:
- Honours

Project Title:Clinical anatomy of the lower limb

The Fogg Lab looks at a wide range of anatomical features and relations, all from a clinical/surgical perspective. These projects utilise a diverse suite of techniques that include advanced dissection, 3D modelling, macrosectioning, and medical imaging (Xray, CT, MR, uCT) and a range of photographic and other visualisation protocols. We aim to provide comprehensive anatomical answers to clinically impactful questions. This project will build upon existing lower limb projects that interrogate regions such as the knee, ankle, foot and hallux. The specific region is subject to Donor availability and arranged in concert with the supervisors and student. These areas suffer from the same lack of reproducible anatomical data, and a level of detail suitable for the demands of modern clinical managament of injuries.

Project Supervisor:
A/Prof Quentin Fogg

Project Availability:
- Honours

Teaching and Learning

Education Group

Contact: Dr Charles Sevigny
Email: sevignyc@unimelb.edu.au
Location: Department of Anatomy and Physiology

Our research interest is in the Scholarship of Teaching and Learning (SoTL) encompassing techniques, strategies and technologies to enhance the learning experiences of undergraduate and graduate students in Anatomy and Physiology. The education research group within Anatomy and Physiology has major focus on student engagement, student experience, and utilising and engagement with technology in learning and teaching. There is focus on utilising current and existing technology, as well as developing new and custom resources, technology, and experiences.

Project: The use of an immersive virtual reality human heart application to improve student learning outcomes

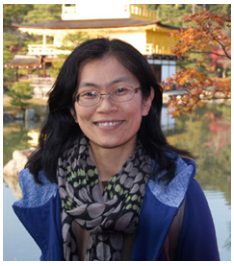
The implementation of virtual reality solutions in biomedical science fields, as well as other STEM fields opens a great number of opportunities for both undergraduate and postgraduate teaching. Recent examinations of virtual reality within the classroom at all levels of education has shown a considerable improvement in student learning outcomes when compared to current teaching methods. This study aims to assess the efficacy of a highly contextual environment for learning in biomedical science. The study will examine whether an immersive environment (virtual reality) will enable better learning outcomes of abstract principles, i.e. the visualisation of the heart and the haemodynamic principles, that are often difficult to replicate in real-life environment. The outcomes from this study will provide evidence of whether immersive learning tools are beneficial for learning abstract concepts in STEM.

Project Supervisor:
A/Prof Sevigny

Project Co-supervisor:
Dr Angelina Fong

Project Availability:
- Honours

Education Group



Contact: Dr Angelina Fong
Email: angelina.fong@unimelb.edu.au
Location: Department of Anatomy and Physiology

Project: Investigating student engagement with online learning and teaching.

Current students are presented with a broad range of learning resources and educational tools. Instructors are keen to integrate a large variety of tools and resources for students with the underlying intent of improving the educational outcomes. The intention of these resources and activities are usually rooted in improving the educational and learning outcomes, or developing transferrable skills in students to improve their future prospects as defined by the graduate attributes. However, it is not clear exactly how students interact and engage with the variety of resources available, or if the students perceive these resources as useful.

Thus, proposed projects may include the following topics:

- Investigating student perceptions of group work
- Evaluating student engagement and interaction with online learning resources
- Developing new learning resources and assessing their efficacy in improving student learning
- Identifying and evaluating student misconceptions in Physiology learning.

The exact nature of the research project may be directed by the student's individual interest in discussion with the supervisors.

Project Supervisor:
Dr Angelina Fong

Project Co-supervisor:
Dr Charles Sevigny
Dr Joseph Rathner

Project Availability:
- Honours
- Master of Biomedical Science

Education Group

Contact: Dr Yossi Rathner
Email: joseph.rathner@unimelb.edu.au
Location: Department of Anatomy and Physiology
Website: go.unimelb.edu.au/ej5i

Project: Enhancing the student learning experience: Evaluating the impact of learning design on the student self-efficacy and assessment performance.

The scholarship of teaching and learning encompasses a broad array of educational outcomes. These include student perception of their learning experience and the impact of teaching design on student learning. In the higher education sector, there is increasing pressure to make learning relevant to the workplace. Graduate attributes for degrees will include *soft skills* like 'lifelong learning' and 'communication skills'. There is also an increasing tension between teaching content (what instructors want students to learn) and learning process (how students learn). Typically STEM educators value content over process. Understanding the motivation of students selecting physiology subjects to study could potentially provide insight into how best to design learning activities, and guide instructors in determining what students need to know.

Research projects in SoTL can be driven by student's individual interest but may include (but not limited to):

- Evaluation of the impact of feedback on student assessment results
- Development of tools to enhance student *meta-learning* (self-efficacy)
- Evaluation of learning design approaches on student outcomes
- Development and deployment of online or e-learning resources, and evaluation of their efficacy.
- Analysis of the internal and external factors that predict assessment performance.

Students who undertake projects in SoTL will develop a deeper knowledge in ways of learning. You will also develop research skills, particularly related to writing and designing survey instruments, qualitative analysis of survey results, as well as quantitative statistical analysis.

This project will be suitable for students who are interested in understanding the methodological and ethical issues associated with research *on* people. You will also deepen your understanding of physiology by simply asking the questions "how do we teach physiology?" and "how is physiology relevant to our real-world experience?".

Project Supervisor:

Dr Joseph (Yossi) Rathner

Project co-supervisors

Dr Angelina Fong

Dr Charles Sevigny

Project Availability:

- Honours
- Master of Biomedical Science

Education Group

Contact: Dr Charlotte Clark
Email: charlotte.clark@unimelb.edu.au
Location: Department of Anatomy and Physiology

Project: Reflecting on troublesome knowledge: Does this result in deeper learning?

Troublesome knowledge' (Perkins, 1999) can be described as concepts that are hard for students to understand. These are often associated with 'threshold concepts' (Entwistle, 2003) which represent transformative learning that allows students to move to a further or deeper level of understanding. Through guided reflective tasks, we have encouraged students studying cell biology to identify concepts that they don't understand, describe steps they will take to understand these and then reflect on whether they have achieved the desired learning outcomes. This project will undertake a qualitative analysis of these reflective tasks to explore perceived and actual self-efficacy and the value of reflection on the learning of troublesome knowledge and overcoming threshold concepts. We will also map summative assessment tasks to these concepts and evaluate how well students were able to complete a summative assessment task that relied on their learning of the identified troublesome knowledge. This research project will aim to provide evidence that supports the benefit of reflective practice in learning troublesome knowledge and overcoming threshold concepts in cell biology. This project will also extend existing inventories of threshold concepts in cell biology and develop a theoretical framework that will be able to be applied more broadly across cell biology education to incorporate reflective practice and threshold concept theory.

Project Supervisor:

Dr Charlotte Clark

Project Co-supervisor:

Dr Michelle Rank

Project Availability:

- Honours

Project: Evaluation of existing and/or innovative teaching and learning activities

The scholarship of teaching and learning (SoTL) is a scholarly approach to the evaluation of student learning. The design and delivery of education is often based on traditional modes of teaching and learning. However, The University of Melbourne is constantly striving to enhance and advance its educational offerings. A fundamental aspect of this process is the evaluation of existing teaching and learning activities, the implementation of innovative, evidence-based teaching and learning activities and the subsequent evaluation of these innovations. A number of opportunities exist for passionate scholars of biomedical science to undertake meaningful research into biomedical science education through varied and exciting SoTL projects. Research projects can be developed based on student interest and passion but will generally include a combination of quantitative and qualitative analysis methods which will expose students to a range of relevant biomedical science research methodologies.

Some areas of current research and opportunities for further research include (but are not limited to):

- Evaluating the value of student attendance at face-to-face classes
- Evaluating the role of reflective practice in undergraduate education
- Interrogating LMS analytics to determine what resources students are utilizing and when and how this aids student learning
- Developing tools or processes to facilitate and assess student online collaboration
- Exploring student misconceptions in cell biology (and/or other relevant biomedical sciences)
- Application of design thinking in educational design

Project Supervisor:

Dr Charlotte Clark

Project Co-supervisor:

Dr Michelle Rank

Project Availability:

- Honours

Education Group

Contact: A/Prof Michelle Rank
Email: michelle.rank@unimelb.edu.au
Location: Department of Anatomy and Physiology

Project: What makes a good laboratory manual? Defining core principles of effective practical lab manuals and exploring the impacts on student learning and engagement.

Students likely encounter an enormous variety of practical manual formats in their STEM studies, but the extent of this variability is largely unknown4. What makes a practical manual an effective resource in the first place is still not understood, nor investigated. What resources in these manuals are routinely used by students? Do students find prac manuals helpful in guiding their learning, if so, to what extent? What is the scope of resources utilised, which additional resources can be exploited, and what guidelines can be used to select/design the most effective resources for inclusion? This lack of consensus makes it extremely challenging for educators in STEM disciplines to construct practical manuals with evidence-based design elements that will enhance student learning in a hands-on teaching environment.

This project seeks to define core foundational principles for the design of effective teaching resources for hands-on practical teaching sessions. This essential information will then be used to develop an evidence-based guide, or 'instruction manual', for educators in STEM to create effective practical learning resources, with subsequent validation to occur as part of a separate LTI application.

Project Supervisor:
A/Prof Michelle Rank

Project Co-supervisor
Dr Amber Willems-Jones

Project: Exploring the impact of technology based pedagogical strategies on undergraduate and postgraduate anatomy curricula

The current gold-standard resource for anatomical education is human dissection and examination of specialist prepared dissected human materials. With growing student cohorts and increased availability of high-quality digital anatomical resources such as 3D apps and imaging software, the resources utilised in delivery of anatomy curricula are undergoing a major shift. This anatomy education focused research project will use a cross-institutional approach to compare the efficacy of various undergraduate and graduate clinical anatomy programs. Comparisons will be made across specific resources utilised (ie. digital, haptic models, cadaveric etc.), pedagogical approaches employed, and student learning outcomes achieved. There is scope for this project to be modified based on the interests of the research candidate.

Project Supervisor:
A/Prof Michelle Rank

Project co-supervisor
A/Prof Karena Waller

Dr Elisa Bone

Project availability
- PhD
- Master of Biomedical Science

Project: Team work makes the dream work: developing new interprofessional student informed teaching resources for improved clinical training pathways.

This project represents a collaboration between the disciplines of Anatomy and Physiology (School of Biomedical Sciences), Audiology (School of Health Sciences), and Speech Pathology (School of Health Sciences). This is a multi-staged project which aims to enrich and improve learning in applied anatomy for students undertaking clinical training from first-year, through to second-year clinical placements and finally to continuing professional development for graduating clinicians. The primary objectives of this study are to better understand the "pinch points" for students learning anatomy and physiology both before and during their clinical placements. There is currently an urgent unmet need to develop effective digital teaching resources, in collaboration with students, that can be utilised by students in their clinical training pathways to study essential anatomical knowledge and the associated physiology. This project will survey students before, during, and after their clinical training, develop a new learning resource in collaboration with clinical trainees, and evaluate the teaching innovations against successful learning before, during, and after students undertake their applied clinical training.

Project Supervisor:
A/Prof Michelle Rank

Project Co-Supervisor:
A/ Prof Bryony Nayagam.

Project Availability:
- Honours

Project: What makes a good laboratory manual? Defining core principles of effective practical lab manuals and exploring the impacts on student learning and engagement.

Students likely encounter an enormous variety of practical manual formats in their STEM studies, but the extent of this variability is largely unknown4. What makes a practical manual an effective resource in the first place is still not understood, nor investigated. What resources in these manuals are routinely used by students? Do students find prac manuals helpful in guiding their learning, if so, to what extent? What is the scope of resources utilised, which additional resources can be exploited, and what guidelines can be used to select/design the most effective resources for inclusion? This lack of consensus makes it extremely challenging for educators in STEM disciplines to construct practical manuals with evidence-based design elements that will enhance student learning in a hands-on teaching environment. This project seeks to define core foundational principles for the design of effective teaching resources for hands-on practical teaching sessions. This essential information will then be used to develop an evidence-based guide, or 'instruction manual', for educators in STEM to create effective practical learning resources, with subsequent validation to occur as part of a separate LTI application.

Project Supervisor:

A/Prof Michelle Rank

Project Co-Supervisor:

Dr Amber Willems-Jones

Project Availability:

- Honours
- PhD
- Masters of Biomedical Science

Exploring the impact of technology based pedagogical strategies on undergraduate and postgraduate anatomy curricula.

Project Description: The current gold-standard resource for anatomical education is human dissection and examination of specialist prepared dissected human materials. With growing student cohorts and increased availability of high-quality digital anatomical resources such as 3D apps and imaging software, the resources utilised in delivery of anatomy curricula are undergoing a major shift. This anatomy education focused research project will use a cross-institutional approach to compare the efficacy of various undergraduate and graduate clinical anatomy programs. Comparisons will be made across specific resources utilised (ie. digital, haptic models, cadaveric etc.), pedagogical approaches employed, and student learning outcomes achieved. There is scope for this project to be modified based on the interests of the research candidate.

Project Supervisor:

A/Prof Michelle Rank

Project Co-Supervisor:

Dr Karena Waller

Dr Elisa Bone

Project Availability:

- Honours
- PhD
- Masters of Biomedical Science

Affiliated Research Groups

Ackland Group

Contact: A/Prof 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: Surgical repair of the distal biceps tendon: A biomechanical study

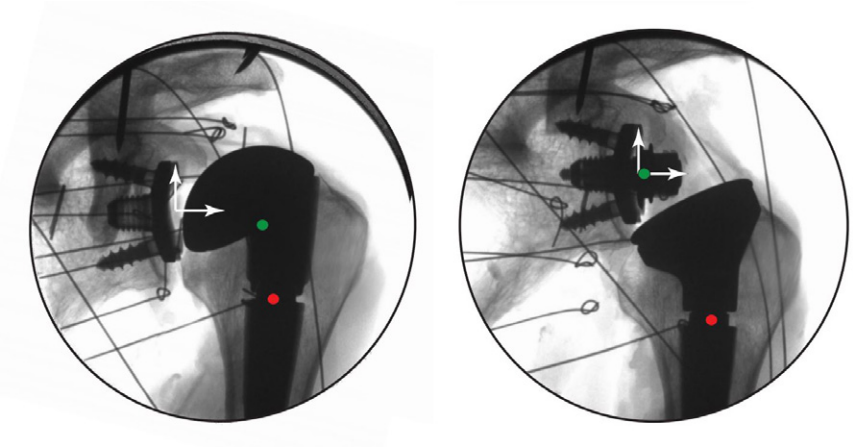
Distal biceps tendon injuries include acute complete and partial ruptures as well as chronic ruptures. In general, surgical treatment is recommended for most patients in order to restore normal muscle strength and function, particularly during forearm rotation-based activities. Different repair techniques have been described that utilise bone tunnels, interference screws, anchors, and cortical buttons (endobutton). This study aims to investigate the biomechanical properties of a novel distal biceps repair technique with two endobuttons deployed, and compare the results to that of a conventional interference screw-based repair method. The findings will have implications for clinical use and outcome of this surgical method.

Project Supervisor:

- A/Prof David Ackland

Project Availability:

- 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 iPSC-derived organoids to understand oligodendrocyte biology

Our understanding of oligodendrocyte biology and myelination stems mostly from mouse studies. We have generated organoids using human iPSC which contain myelinating oligodendrocytes thereby allowing us to further our understanding of oligodendrocytes and myelination, in a human context, both in development and in disease.

Project Supervisor:
Dr Samantha Barton

Project Co-supervisor:
Georgina Craig

Project Availability:
- Master of Biomedical Science
- Honours

Project: Testing novel drugs on our human IPSC-derived organoid model of multiple sclerosis

Project Description: Multiple sclerosis (MS) is characterised by sporadic autoimmune attacks on myelin, the lipid dense sheath that encases neuronal axons. To date, no drugs that have been identified in mouse models of MS to promote repair and regeneration of this myelin sheath have translated through to the clinic. This therefore highlights the need for improved model systems for biological interrogation into these processes as well as for drug screening.

Project Supervisor:
Dr Shwathy Ramesan

Project Co-supervisor
Ms Katie Lewis

Project Availability:
- Master of Biomedical Science
- 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

Project Availability:

- Honours

Cheng Group

Contact: A/Prof Louise Cheng
Email: louise.cheng@petermac.org
Location: Victorian Comprehensive Cancer Centre

Project: How do tumours grow at the expense of other tissues in cancer cachexia

Cancer cells are known to drive altered metabolic circuits to meet the bioenergetic and biosynthetic demands of increased cell growth and proliferation. Under nutrient restriction, when growth of most organs shut down, cancer cells can bypass these brakes imposed on cellular growth, thus gaining a growth advantage under these conditions. Furthermore, during cachexia, which causes more than one third of cancer death, tumour derived factors can also induce the break down of fat and skeletal muscles, in order to generate metabolic intermediates necessary for the preferential tumour growth. The signalling between tumours and other tissues is highly complex, and the adaptations that allow cancer cells to preferentially activate growth are largely unknown. The student will work within a existing team to discover some of the mediators of cancer cachexia using Drosophila genetics, confocal microscopy, proteomics, metabolomics; the findings will be further validated in human samples.

Project Supervisor:
A/Prof Louise Cheng

Project co-supervisor
Dr Callum Dark

Project Availability:
- Honours
- Master of Biomedical Science

Project: Non-autonomous regulation of tumour growth

How tumours communicate with tissues to trigger their breakdown is a key unresolved question. We have generated novel genetic tools that allow independent spatial and temporal overexpression or knockdown of genes in multiple tissues simultaneously. Using these tools, this project aims to look at how brain tumours can interact with other tissues.

Project Supervisor:
A/Prof Louise Cheng

Project Availability:
Honours

Eckersley-Maslin Group

Contact: Dr Melanie Eckersley-Maslin
Email: melanie.eckersley-maslin@petermac.org
Location: Victorian Comprehensive Cancer Centre

The Eckersley-Maslin (EckMas) laboratory investigates epigenetic plasticity in both developmental and cancer models. We use insights from development, where cell identity is tightly controlled and regulated, to understand how cell identity is established and maintained, to get new insights into how cell identity becomes deregulated in pathologies such as cancer.

Project: Features of bivalent chromatin in development and cancer

Bivalent chromatin occurs at regions of DNA, bound to histone proteins, that has both activating and repressive marks. The co-occurrence of these two marks is thought to hold the DNA sequence in a primed or poised state for future activation or silencing. Bivalent chromatin is best understood in stem cells where it is most abundantly found, however cancer cells have also been described to have bivalent chromatin. Crucially, we do not know how bivalent chromatin is targeted to specific DNA regions, how it changes during tumourigenesis and whether it promotes aspects of cancer biology.

The aim of this project is to characterise bivalent chromatin in both stem cell and cancer cell models to further understand the dynamics and importance of this unique molecular structure. This project will use a novel unpublished method developed in the lab to profile bivalent chromatin. The project will use stem cell and cancer cell lines with an option to apply this method to patient samples. A range of cell and molecular biology techniques will be used including epigenomics, next generation sequencing and stem cell and cancer cell culture.
The study will involve both wet-lab and bioinformatic analysis of datasets generated in this project.

Project Supervisor:

Dr Melanie Eckersley-Maslin

Project Availability:

- Honours

Project: Using novel biosensors to investigate bivalent chromatin in stem cells and cancer

A major challenge in eliminating cancer is its inherent plasticity. Research in our lab uses insights from development to give new perspectives into how cancer cells acquire heightened plasticity in the absence of additional genetic mutations. One example of epigenetic plasticity is bivalent chromatin, characterised by the co-occurrence of both activating and repressive histone modifications on the same chromatin fragment. It is typically found at gene promoters and thought to hold these sequences in a poised state for future expression or silencing. Crucially we do not understand the molecular regulation of bivalent chromatin hampering our ability to target this feature of plasticity.

This project aims will use a novel unpublished biosensor developed in the lab to detect bivalent chromatin in single cells. The project will generate reporter stem cell and cancer cell lines to visualise the distribution and dynamics of bivalent chromatin in living cells. CRISPR-mediated screens will then uncover regulators of bivalent chromatin. The study will involve both wet-lab and bioinformatic aspects and employ a range of techniques including cell culture, molecular cloning, flow cytometry, microscopy, CRISPR-screening, epigenomics and bioinformatics. This discovery-project will reveal new insights into epigenetic plasticity required to develop future therapeutic strategies targeting cancer cell plasticity.

Key words: Epigenetics, Cancer Cell Biology, Chromatin, Plasticity, Bivalent, Next Generation Sequencing, gene expression, stem cell biology

Primary Supervisor:

Dr Melanie Eckersley-Maslin

Co-supervisor:

Dr Katie Fennell

Project Availability:

- PhD.

Project: Exploring the significance of early embryonic transcriptional signatures in cancer

Embryonic development shares several similarities with cancer development. We leverage this parallel, using our knowledge of how embryos grow to understand how cancers arise from healthy adult cells. Both embryogenesis and tumorigenesis involve changing cell identity and an increase in cellular plasticity. We have recently uncovered a transcriptional signature of plasticity. This signature is upregulated during times of heightened plasticity in the earliest stages of embryonic development. Excitingly, some cancers also express this embryonic transcriptional signature of plasticity. And when they do, this is often associated with worse outcomes for patients in terms of survival.This project will employ bioinformatic analyses to further uncover the significance of this signature of plasticity across a range of different cancer types and stages, investigating its use as a potential biomarker. We will use motif analyses and other analyses to reveal potential drivers of this transcriptional signature and (for longer projects) test them experimentally using CRISPR-activation and/or overexpression systems in cancer cell lines. Many of the transcripts in the signature have not been characterised and their molecular functions remain unknown. The project may also explore whether the transcripts may have additional functional roles in the cell in promoting cancer processes. Techniques for this project include bioinformatics, cell culture, RNA extraction and analysis (using quantitative real-time PCR or RNA-sequencing), cloning, CRISPR-activation and other CRISPR-based technologies, and in vitro cancer cell assays. The project would suit an honours/masters student interested in bioinformatics (analysis only) or a PhD student interested in mastering both bioinformatics and experimental biology.

Primary Supervisor:

A/prof Michelle Rank

Co-supervisor:

A/Prof Bryony Nayagam

Project Availability:

- PhD
- 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

Project Availability:

- PhD
- 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

Project Availability:

- PhD
- Honours
- Master of Biomedical Science

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

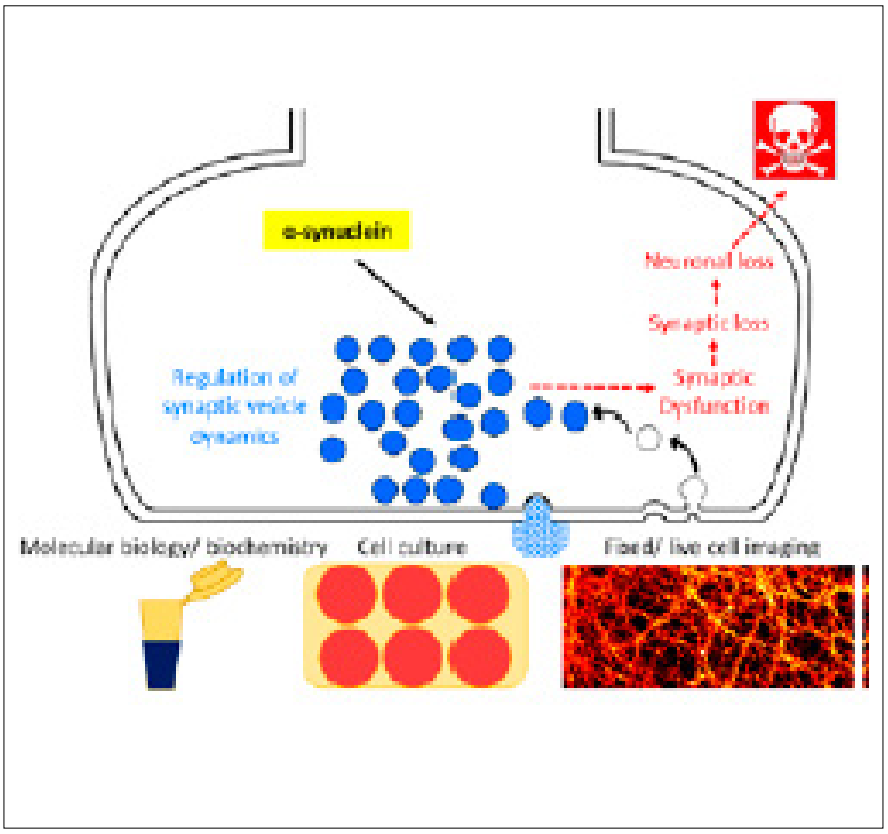
We have recently identified novel sites in alpha synuclein that are phosphorylated in an activity-dependent manner. This project will ascertain how phosphorylation at these distinct residues modulates the function of alpha synuclein as a regulator of presynaptic activity.

Project Supervisor:

Dr Sarah Gordon

Project Availability:

- PhD
- Honours
- Master of Biomedical Science



Hannan Group

Contact: Prof. Anthony Hannan
Email: anthony.hannan@florey.edu.au
Location: Florey Institute of Neuroscience and Mental Health
Website: go.unimelb.edu.au/w65i
go.unimelb.edu.au/c65i

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:
Prof Anthony Hannan

Project Co-supervisor:
Dr. Carolina Gubert

Project Availability:
- M.Phil/PhD
- 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

Project Availability:

- M.Phil/PhD
- 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:

Dr Emma Burrows

Project Co-supervisor

Prof Anthony Hannan

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science

Project: Cognitive, social and psychiatric behavioural traits and their pharmacological treatment in a mouse model of neurofibromatosis type I

Patients suffering from neurofibromatosis type 1 have a mutation in one allele of the neurofibromin 1 (NF1) gene, leading to a variable clinical presentation which may include the formation of tumours, hyperpigmentation marks, vision disorders and scoliosis. However, patients also typically show a range of neuropsychological symptoms including cognitive impairments and learning difficulties, attention deficits, as well as autism and depression. Despite the profound impact on the lives of patients and their families, these symptom complexes remain inadequately addressed by current treatments.Nf1 +/- mice used in this project are a widely used model for neurofibromatosis type 1, though the study of cognitive and psychiatric behavioural traits has been limited to date and warrants further investigation. The initial approach will involve the phenotypic characterisation of this mouse model using a broad battery of state of the art rodent behavioural tests, with the aim of examining specific aspects of cognition and attention, social function, as well as anxiety-like and depression-like behaviour. This will include the use of rodent touchscreen tests, which are directly translatable to human patients. In parallel, biochemical and molecular techniques will be used to investigate the brain mechanisms underlying the behavioural deficits observed in these mice. This will be followed by the application of promising drug candidates in a preclinical study using the Nf1 +/- mouse line, with the aim of progressing successful candidates to a clinical study in the near future with our clinical collaborators in Parkville.

Project Supervisor:

Prof Anthony Hannan

Project Co-supervisor

Dr Huan Liao
Dr Sonali Reisinger

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science

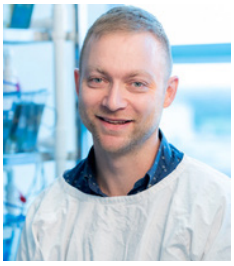
Project: Investigating multigenerational effects of paternal immune activatoin on brain function

Brain disorders account for a significant global burden of disease, yet the “missing heritability” in common brain disorders like autism, schizophrenia, depression, and anxiety suggests the involvement of environmental factors, including paternal exposures before conception. This project aims to explore the impact of paternal pathogenic infections on epigenetic inheritance and offspring phenotypes, representing a paradigm shift in understanding the intergenerational effects of pathogens on public health.

Recent research has revealed the potential of pathogens to influence paternal germ cell epigenetics and modify offspring phenotypes, highlighting the urgent need to investigate the intergenerational impacts of paternal infection on brain development, behavior, and cognition. This is particularly relevant in the context of the ongoing COVID-19 pandemic.

While maternal immune activation’s impact on offspring brain function has been studied, the influence of immune activation in the male germline and subsequent offspring phenotypes remains unexplored. A pioneering study by our team demonstrated epigene,

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.

Projects: 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. In recent decades, analysis of vascular cell fates, such as artery, vein and lymphatic fates, has uncovered key transcription factors and target enhancer elements that regulate tissue identity. Nevertheless, 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. Transgenesis, molecular genetics and cellular resolution confocal imaging of zebrafish vasculature will be coupled with bioinformatics studies of enhancer conservation and prediction of key functional regulators.

Project Supervisor:

Prof Ben Hogan

Project Co-supervisor:

Dr Lizzie Mason

Project Availability

- Honours
- Master of Biomedical Science

Project: 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

Project Availability

- 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

Project Availability

- Honours
- Master of Biomedical Science

Hossain Group

Contact: A/ Prof M Akhter Hossain
Email: akhter.hossain@unimelb.edu.au
Location: Florey Institute of Neuroscience and Mental Health

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.

Project: Developing INSL5 analogs as colon motility regulator

The gut hormone insulin-like peptide 5 (INSL5) is an endogenous ligand for the G protein-coupled receptor RXFP4 that is present in the enteric nervous system. Our recent compelling data suggest that INSL5 regulates colonic motility and has the potential for treating chronic constipation, a major unmet medical need that is associated with significantly reduced quality of life and morbidity. However, INSL5 has a complex insulin-like structure which is difficult to synthesise making it not readily available. In a major advance, we recently developed the first potent and highly selective peptidomimetic agonist and antagonist of RXFP4 which are significantly easier to assemble in large quantities compared with native INSL5.

In this project, we will both optimise our lead peptides (agonist and antagonist) and develop novel single-B-chain mimetics by using our novel pi-pi 'stapling method'. We will validate the actions of the novel RXFP4 peptide agonists and antagonist both in vitro and in vivo. We will also utilise two mouse models of constipation, diarrhea and RXFP4 knockout mice for investigating RXFP4-mediated colon motility. Our innovative project will result in a novel research tool and drug lead, and the outcomes will validate the INSL5-RXFP4 system as a target for the treatment of constipation and diarrhea.

Project Supervisor:
A/Prof M. Akhter Hossain

Project Co-supervisor:
Dr Ruslan Pustovit
Dr Mengjie Liu

Project Availability:
- Honours
- Master of Biomedical Science

Lankadeva Group

Contact: Dr Yugeesh Lankadeva
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Location: Florey Institute of Neuroscience

Sepsis is the leading cause of death in intensive care units and contributes to ~11 million deaths worldwide annually. Septic patients present with circulatory and metabolic abnormalities that substantially increase their mortality.

Current patient management involves restoring blood pressure with vasopressors, primarily noradrenaline. However, most septic patients become unresponsive to noradrenaline leading to refractory hypotension. We recently discovered that mega-dose vitamin C fully restored sensitivity to noradrenaline, improved blood pressure management and protected vital organs including the brain and kidneys from acute injury. In this project, we aim to investigate the mechanisms by which mega-dose vitamin C reverses the microcirculatory dysfunction by using a range of in vivo, in vitro and molecular techniques using a clinically relevant sheep model of sepsis.

Project: Delineating the vascular mechanisms by which mega-dose vitamin C reverses cerebral and renal microcirculatory dysfunction during sepsis.

In this project, we aim to investigate the mechanisms by which mega-dose vitamin C reverses the microcirculatory dysfunction by using a range of in vivo, in vitro and molecular techniques using a clinically relevant sheep model of sepsis

Project Supervisor:

Dr Yugeesh Lankadeva

Project Co-supervisor:

Dr Ash Betrie
A/Prof Scott Ayton

Project Availability:

- Master of Biomedical Science
- Honours

Pan Group

Contact: Dr Nicholas Pan
Email: yijun.pan@unimelb.edu.au
Location: Florey Institute of Neuroscience and Mental Health

Project:Can we identify novel biomarkers for early detection of Alzheimer's disease (AD) by targeting the brain-draining lymph nodes?

Alzheimer's disease (AD) affects >55 million people globally, placing a heavy socioeconomic burden on all countries. The majority of clinical trials for the treatment of AD have reported minimal benefits. One of the major reasons was that the recruited patients were at late disease stage with irreversible damage to the brain. They have also shown that better therapeutic outcomes can be achieved in earlier AD stage.

Project Supervisor:

Dr Nicholas Pan

Co-supervisor

Prof Colin Masters and Dr Liang Jin

Project Availability:

- Masters of Biomedical Science
- Honours
- PhD

Project: Exploring the role of fatty acid-binding proteins in microglia immunometabolism

Microglia are the resident immune cells in the central nervous system (CNS). They interact with the CNS microenvironment through different molecules such as chemokines, cytokines, and trophic factors which, in turn, modulate microglia activities converting the homeostatic microglia into activated microglia (broadly defined as proinflammatory and anti-inflammatory) and vice versa. By transforming between a spectrum of phenotypes, microglia can clear cell debris through phagocytosis, stimulate repair and regeneration of neurons, and maintain the homeostasis in the CNS. The microglia immune phenotype transformation is supported by cellular metabolism reprogramming. Given the tight relationship between immune function and metabolism in microglia, they are often collectively referred to as immunometabolism. Fatty acid-binding proteins (FABPs) are a family of intracellular proteins involved in cell metabolism. We have confirmed the presence of FABP3, 4, and 5 isoforms in microglia, however, their roles in the microglia are not clearly defined. In this project, we will use CRISPR-Cas9 genome editing, in vivo cross linking, proteomics, single-cell RNA sequencing, automated high throughput metabolism profiling, magnetic activated cell sorting, transgenic mouse models and human microglia to explore the roles of FABPs in microglia immunometabolism, and potential involvement in neurodegernative diseases.

Note: Students involved in this project will be offered opportunity to perform medium/short-term experiments in Japan.

Project Supervisor:

Dr Nicholas Pan

Co-supervisor

Dr Ben Gu and Liang Jin

Project Availability:

- Masters of Biomedical Science
- Honours
- PhD

Project: Can we achieve precise medication use in people living with Alzheimer's disease?

Alzheimer's disease (AD) is the most common form of dementia, affecting 1 in 9 people >65 years. AD is featured by progressive neuron loss in the brain and decline in cognitive function. However, recent evidence suggests that AD may also affect peripheral organs. In line with this, we have for the first time demonstrated that the expression and function of drug transporters and metabolising enzymes in the peripheral organs are altered in AD mouse models, leading to altered drug disposition. Some of these changes have been validated in AD human tissues, however, if drug disposition is affected in people with AD is yet to be determined. Polypharmacy, or the use of multiple medications, is prevalent in older populations and people with AD are prescribed 5-10 more medications than their peers. This heightened polypharmacy places people with AD at a greater risk of adverse drug reactions (ADRs), particularly if the disease alters the drug disposition. For nearly all medications, medical practice is based on single disease guidelines derived from clinical trials that do not include people with AD. If drug disposition is altered in AD, a standard dose may produce unexpected therapeutic outcomes (e.g. increased risk of ADRs) in people with AD. People with cognitive impairment are also less likely to report ADRs, which presents an additional challenge in caring for people with AD and is likely to lead to suboptimal healthcare outcomes.

In this project, we will use high-throughput proteomics to profile drug transporter and drug metabolising enzyme expression in AD and non-AD human tissues, leading to the development of a physiologically based pharmacokinetic models for dose adjustment in people with AD. These models will be validated using plasma samples collected via Australian Imaging, Biomarker & Lifestyle (AIBL) study of aging. The ultimate goal of this research program is to achieve precise medication use in people with AD.

Project Supervisor:

Dr Nicholas Pan

Co-supervisor

Dr Liang Jin and Prof Colin Masters

Project Availability:

- Masters of Biomedical Science
- Honours
- PhD

Project:Can we improve drug delivery in glioma?

Drug delivery into the brain is regulated by the blood–brain interfaces, including the blood–brain barrier (BBB) and the blood–cerebrospinal fluid barrier (BCSFB). These selective barriers present a high impermeability to most substances, with the selective transport of nutrients and transporters preventing the entry and accumulation of possibly toxic molecules, comprising many therapeutic drugs. Transporters of the ATP-binding cassette (ABC) superfamily have an important role in drug delivery, because they extrude a broad molecular diversity of xenobiotics, including several anticancer drugs, preventing their entry into the brain. Gliomas are the most common primary tumors diagnosed in adults, which are often characterized by a poor prognosis, notably in the case of high-grade gliomas. Therapeutic treatments frequently fail due to the difficulty of delivering drugs through the brain barriers, adding to diverse mechanisms developed by the cancer, including the overexpression or expression de novo of ABC transporters in tumoral cells and/or in the endothelial cells forming the blood–brain tumor barrier (BBTB). In this project, we will explore the impact of glioma pathology on the signalling pathways regulating ABC transporters, and also other transporters that can be a target to improving drug delivery. For the Honours project, the student(s) will be required to perform bioinformatics analysis on existing clinical data set. For the Masters project, the student will perform proteomics analysis on human glioma tissues, and subsequent bioinformatic analysis. In addition, the student will be required to compare our dataset with those published in omics database.

Project Supervisor:

Dr Nicholas Pan

Co-Supervisor

Dr Liang Jin

Project Availability:

- Masters of Biomedical Science
- PhD

Project:Exploring the genetics links between Alzheimer's disease and type 2 diabetes

There is a considerable body of literature on associations between type 2 diabetes (T2D) and Alzheimer's disease (AD). It has been calculated in a meta-analysis that individuals with T2D were 39% more likely to develop AD than non-diabetics. Pathophysiologically this relationship between T2D and AD has not been completely elucidated. Insulin resistance in T2D has been shown to exacerbate directly amyloid and tau pathologies, and their shared pathophysiological traits of synaptic dysfunction, inflammation, and autophagic impairments. In this study, we aim to determine if a genetic link exist between AD and T2D to improve our understanding of the shared pathways. The students will have access to the genetics data collected via The Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL), and will be provided training on genetic analysis.

Project Supervisor:

Dr Nicholas Pan

Co-Supervisor

Dr Liang Jin

Project Availability:

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

Project:Explorating the link between Alzheimer's disease and co-morbidities

A wide range of comorbid diseases is associated with Alzheimer's disease (AD), the most common neurodegenerative disease worldwide. Evidence from clinical and molecular studies suggest that chronic diseases, including diabetes, cardiovascular disease, depression, and inflammatory bowel disease, may be associated with an increased risk of AD in different populations. Disruption in several shared biological pathways has been proposed as the underlying mechanism for the association between AD and these comorbidities. Since 2006, our group has started a large cohort study in Australia - The Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL), the collected data is >18000 participant-years. In this project, 2 motivated students are required to perform literature review and take advantage of our collected data from AIBL (and possible other 7 leading AD cohorts in the world) to improve our understanding in the association between AD and comorbidities from epidemiology and/or perspectives.

Project Supervisor:

Dr Nicholas Pan

Co-Supervisor

Dr Liang Jin

Project Availability:

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

Renoir Group

Contact: Dr Thibault Renoir
Email: thibault.renoir@florey.edu.au
Location: Florey Institute of Neuroscience and Mental Health

Project: Modulating metals homeostasis to treat neurodegenerative and psychiatric disorders

While iron dyshomeostasis (i.e. elevated iron) is known to be linked to some neurodegenrative diseases (e.g. Huntington's disease), no study has yet attempted to modulate iron metabolism in psychiatric disorders.

Project Supervisor:
Dr Thibault Renoir

Co-supervisor
Prof Tony Hannon

Project Availability:
- Masters and Honours

Project: Gene-environment interactions in the regulation of cellular plasticity, cognitive function and behaviour

By integrating wide-ranging expertise (including animal behaviour, electrophysiology and molecular/cellular skills) this project explores how genes and environment combine via experience-dependent plasticity in the healthy and diseased brain.

Project Supervisor:
Dr Thibault Renoir

Co-supervisor
Prof Tony Hannon

Project Availability:
- Masters and Honours

Project: Do the beneficial effects of exercise involve miRNA-mediated regulation of gene expression?

Although exercise is known to delay symptom onset and progression in a variety of neurological and psychiatric conditions, the mechanisms underlying these effects remain poorly understood. A notable candidate molecular mechanism is that of microRNA, a family of small noncoding RNAs that are important regulators of gene expression.

Project Supervisor:
Dr Thibault Renoir

Co-supervisor
Prof Tony Hannon

Project Availability:
- Masters and Honours

Project: Therapeutic psychedelics in mental health

Psychedelics have recently re-emerged as promising therapeutics for several neuropsychiatric disorders. Clinical studies have confirmed the efficacy of ketamine for the treatment of depression and suggest potential therapeutic properties of psilocybin, a naturally occurring psychedelic prodrug produced by more than 200 fungi. While psychedelics could transform the landscape of treatments for many disorders, this field of research is still in its infancy. One of the main problems at the heart of modern psychedelic clinical research is that participants might easily be able to tell whether they have been given a placebo as compared to receiving hallucinogenic compounds. In this regard, preclinical studies harbor several advantages including the possibility to conduct well-controlled experiments as well as using innovative tools to better understand the biological mechanisms mediating the behavioural effects. However, only a few studies have examined the effects of psilocybin in rodent disease models.

Project Supervisor:
Dr Thibault Renoir

Co-Supervisor
Prof Tony Hannan

Project Availability:
- Honours
- Master of Biomedical Science
- PhD

Reid Group

Contact: Prof Chris Reid
Email: christopher.reid@unimelb.edu.au
Location: Florey Institute of Neuroscience and Mental Health

Project: Using in vitro and in vivo models to understand mechanisms underlying epilepsy and test treatments

Epilepsy is a devastating disease with approximately 30% of patient's seizures not controlled using current anti-seizure medication. Clinicians and geneticists have identified the genetic cause of a large proportion of severe epilepsy. From this information we can build models that mimic the human genetic changes. These experimental models provide important pathways that will help patients with severe epilepsy and act as tools for understanding mechanisms. In our laboratory, we can interrogate the disease models using molecular, electrophysiological and behavioural techniques to better understand what causes seizures. From this, we develop ideas on how to fix what is broken—creating precision medicines. These can be small molecules or genetic therapies. We then go back to our experimental models and test these ideas. We work with clinicians who are leaders in the epilepsy field to translate our findings to patients. Our goal is to help epilepsy patients live seizure-free lives.

Project Supervisor:
Prof Chris Reid

Project Co-supervisor:
Prof Ian Foster

Project Availability:
- Honours
- Master of Biomedical Science
- Phd

McColl Group

Contact: Dr. Gawain McColl
Email: gmccoll@unimelb.edu.au
Location: Kenneth Myer Building
Website: 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:Support Cells and Dopaminergic Neurons

Project Description: The levels of iron in the brain increases significantly during ageing and is even further elevated in Parkinson's disease. While iron is essential for normal cell and nerve function, elevated iron levels within these cells may be a trigger for cell death. We are exploring how dopaminergic neuron cells are supported by closely associated glial cells, and the role glia play in regulating iron within the dopaminergic neuron cells. Understanding how the interactions between iron, glia and dopamine change through lifespan may provide new avenues for interventions to prevent cell death in Parkinson's disease.

Project Supervisor:

Dr Gawain McColl

Project Availability:

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

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

Project Availability:

- 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

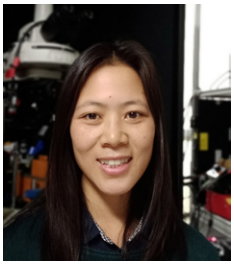
Project co-supervisor

Prof. Ashley Bush

Project Availability:

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

Mo Group



Contact: Dr Christina Mo
Email: christina.mo@unimelb.edu.au
Location: Florey Institute of Neuroscienc

Project:Identifying and manipulating the neural circuits of decision-making

Making choices is a part of daily life yet one of the most challenging but fascinating questions in neuroscience is the neural basis of decision-making. Decision-making arises from activity between cortical areas but this communication also occurs via higher order thalamus. These cortico-thalamo-cortical pathways ubiquitously parallel direct corticocortical pathways in the brain, yet their role in perception has largely been ignored. Our previous work has shown that the transthalamic pathway in the somatosensory system is an essential neural pathway for perceptual decisions (Mo et al., 2023, PMID: 37034798). This project delves deeper into the role of transthalamic pathways in perceptual choice by combining trans-synaptic tracing (rabies virus), live calcium imaging (miniscopes) and controlled silencing or activation of neural circuits (optogenetics) during a behavioral task. Students with experience in mouse behaviour, coding or an interest in neural circuits are encouraged to apply.

Project Supervisor:

Dr Christina Mo

Project Availability:

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

McDougall Group

Contact: Dr Stuart McDougall
Email: stuart.mcdougall@florey.edu.au
Location: Florey Institute of Neuroscience and Mental Health

The McDougall/Viserosensory lab at the Florey Institute studies the basic neurophysiology underpinning the integration of sensory information within the brain.

Our focus of study is at the level of the brain that first receives signals from visceral organs including those of the cardiorespiratory and gastrointestinal systems. This basic knowledge gained is pertinent to several disease states including hypertension and obesity, and mental health. The primary techniques utilised within the laboratory revolve around anatomical mapping using viral tools in combination with in vitro slice electrophysiology. We possess a large skill set and toolkit to answer a variety of experimental questions including optogenetics through to behavioural paradigms.

Project:Marry the ascending central pathways from the brainstem to their sensory vagal input.

The vagus nerve, which connects the brain with most of the thoracic and abdominal organs, contains the axons of sensory vagal afferent neurons and their central terminals that synapse in brainstem. After synapsing in the brainstem, viscerosensory information is distributed widely throughout the brain, including to brainstem nuclei associated with autonomic control and pontine and forebrain structures some associated with appetite. Here we will define the vagal sensory input to defined NTS projection neurons (ie NTS to the arcuate hypothalamus). This is achieved using a Cre-dependent monosynaptic rabies tool.

Project Supervisor:
Dr Stuart McDougall

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

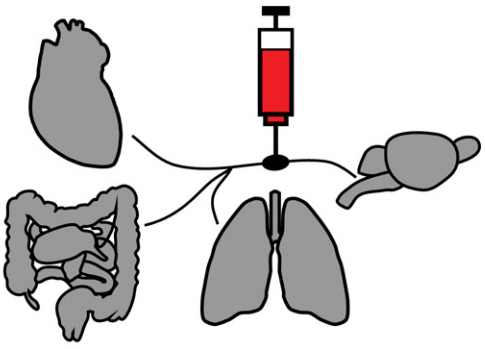
Project: Optogenetic activation of vagal afferents to decode viscerosensory signal processing within the brain.

How different sensory signals from internal organs are organised and processed upon first entering the brain is ill defined. Viscerosensory signals arise from several functional modalities; baroreceptors, chemoreceptors, lung stretch afferents, gastrointestinal etc. These varied signals all terminate in the solitary nucleus with overlapping terminal fields. **Project:** You will use optogenetic tools, that allow for the selectively activation of vagal sensory neurons, to unravel how signals from these different sensory modalities 'talk' to the brain using in vito slice electrophysiology. Optogentic and electrical activation will be compared to further understand to functional determine how the local circuits are organised. This work will be highly relevant to current and future strategies to manipulation behaviour and/or autonomic function.

Project Supervisor:
Dr Stuart McDougall

Project Co-supervisor:
Professor Andrew Allen

Project Availability:
- PhD
- Master of Biomedical Science
- Honours



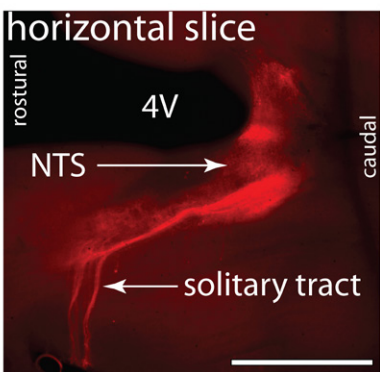
Project: Do vagal afferents synapse at parasympathetic motor neurons within the brainstem.

Sensory signals from internal organs are organised and processed upon first entering the brain is ill defined. Viscerosensory signals arise from several functional modalities; baroreceptors, chemoreceptors, lung stretch afferents, gastrointestinal etc. These varied signals terminate in the solitary nucleus to initiate autonomic reflexes to change internal organ function. **Project:** We have observed terminations in other brain regions too. Here you will use optogentictic tools and slice electrophysiology to determine if vagal afferents synapse at parasympathetic motor neurons. If so, this will redefine autonomic reflex circuitry as we know it.

Project Supervisor:
Dr Stuart McDougall

Project Co-supervisor:
Professor Andrew Allen

Project Availability:
- Master of Biomedical Science
- Honours



Mitto Group

Contact: Dr Remika Mito
Email: remika.mito@florey.edu.au
Location: Florey Institute of Neuroscienc

Project:Using new MRI technologies to detect sports-related concussion

Project Description: In this project, we aim to investigate whether advanced diffusion MRI techniques can detect brain abnormalities in individuals with a recent sports-related concussion (mild Traumatic Brain Injury). This project will take advantage of a recently acquired advanced neuroimaging dataset, and will involve translation of specialised imaging techniques into individualized assessment. We will assess whether these advanced imaging tools, which have proven sensitive at a group-level, can detect brain changes associated with concussion in individual patients and track brain changes over time, from symptom onset to recovery.

Project Supervisor:

Dr Remika Mito

Project Co-supervisor:

A/Prof Heath Pardoe

Project Availability:

- Honours

Project:Neuroanatomical correlates of spatial memory in Australian Football League players

Project Description Australian rules football is a fast-paced contact sport that involves complex decision making and spatial orienting around all 360 degrees of a playing field. In this project, we aim to investigate the neuroanatomical correlates of spatial memory in Australian rules football players. This project will take advantage of a recently acquired advanced neuroimaging dataset, and will use state-of-the-art brain volumetry techniques. This project will examine brain structural changes, with a particular focus on the hippocampus, which is known to play a key role in spatial orientation and memory. The project will be best suited to students with an interest in brain imaging and clinical neuroscience.

Project Supervisor:

Dr Remika Mito

Project Co-supervisor:

A/Prof Heath Pardoe

Project Availability:

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

Nisbet Group

Contact: Dr Rebecca Nisbet
Email: rebecca.nisbet@florey.edu.au
Location: Florey Institute of Neuroscience and Mental Health

Development of novel therapeutic antibodies targeting Tau

Alzheimer's disease (AD) and related dementias, are the leading cause of death of Australian women and the second leading cause of death of Australian men. This is currently no effective treatment for the disease. One of the main pathological hallmarks of AD is the hyperphosphorylation and accumulation of a protein called, Tau, in neurons. Preventing tau aggregation is therefore an attractive therapeutic strategy. Targeting tau is difficult, however, as an effective therapeutic must be able to cross the blood-brain barrier and the neuronal membrane to engage tau within the neuronal cytoplasm. Intrabodies are intracellular antibodies, capable of engaging intracellular targets, such as tau. This project aims to develop novel tau intrabodies and characterise their expression and functionality within neurons. Furthermore, to efficiently deliver the intrabodies to the cell cytoplasm, nucleic acid encoding the intrabodies will be packaged into delivery vehicles (adeno-associated virus, biological vesicles and/or lipid nanoparticles).

Project Supervisor:

Dr Rebecca Nisbet

Project Availability:

- PhD
- Master of Biomedical Science

Determining efficacy of mRNA-encoded antibody therapeutics for the treatment of Alzheimer's disease

Alzheimer's disease (AD) and related dementias, are the leading cause of death of Australian women and the second leading cause of death of Australian men. This is currently no effective treatment for the disease. One of the main pathological hallmarks of AD is the hyperphosphorylation and accumulation of a protein called, Tau, in neurons. Preventing tau aggregation is therefore an attractive therapeutic strategy. Targeting tau is difficult, however, as an effective therapeutic must be able to cross the blood-brain barrier and the neuronal membrane to engage tau within the neuron. We have generated a novel tau antibody that binds specifically to tau and reduces tau aggregation. To enhance delivery of the antibody to neurons, mRNA encoding the antibody has been packaged within lipid nanoparticles and biological vesicles. Once neurons take up the packaged mRNA, the tau antibody is expressed within the neuron and able to engage tau. This project aims to treat tau transgenic mice with the packaged tau antibody mRNA and determine its ability to improve mouse behaviour and reduce tau brain pathology.

Project Supervisor:

Dr Rebecca Nisbet

Project Availability:

- PhD
- Master of Biomedical Science

Nithianantharajah Group

Contact: A/Prof Jess Nithianantharajah
Email: jess.n@florey.edu.au
Location: Florey Institute of Neuroscience and Mental Health

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.

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

The Synapse Biology & Cognition Laboratory is focused on understanding the critical role synaptic genes and proteins play in establishing and regulating the coordinated wiring and connectivity in the brain, that enables complex cognition and higher order processing in the healthy brain, and in mental disorders where these processes go awry. This project will use in vivo calcium imaging of neural activity using miniscopes in behaving mice during reward-based learning in touchscreen tasks.

Project Supervisor:
A/Prof Jess Nithianantharajah

Project Co-supervisor:
Dr Simon Fisher

Project Availability:
- Honours
- Master of Biomedical Science

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

The Synapse Biology & Cognition Laboratory is focused on understanding the critical role synaptic genes and proteins play in establishing and regulating the coordinated wiring and connectivity in the brain, that enables complex cognition and higher order processing in the healthy brain, and in mental disorders where these processes go awry. This project will develop novel rodent touchscreen tasks to interrogate decision-making in mice, combined with in vivo manipulations (optogenetics, photometry, calcium imaging) to elucidate underlying processes.

Project Supervisor:
A/Prof Jess Nithianantharajah

Project Co-supervisor:
A/Prof Stefan Bode

Project Availability:
- Honours
- Master of Biomedical Science

Project: Molecular and biochemical analysis of novel disease variants in neurodevelopmental disorders

The Synapse Biology & Cognition Laboratory is focused on understanding the critical role synaptic genes and proteins play in establishing and regulating the coordinated wiring and connectivity in the brain, that enables complex cognition and higher order processing in the healthy brain, and in mental disorders where these processes go awry. This project will use advanced protein binding and stability assays to measure the structural and functional impacts of novel synapse gene mutations identified in neurodevelopmental disorders including Autism Spectrum Disorder, Intellectual Disability and schizophrenia.

Project Supervisor:
A/Prof Jess Nithianantharajah

Project Co-supervisor:
A/Prof Daniel Scott

Project Availability:
- Honours
- Master of Biomedical Science

Palmer Group

Contact: A/Prof Lucy Palmer
Email: lucy.palmer@florey.edu.au
Location: Florey 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:
A/Prof Lucy Palmer

Project Co-supervisor:
Dr Marius Rosier

Project Availability:
- M.Phil/PhD
- 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:
A/Prof Lucy Palmer

Project Availability:
- M.Phil/PhD
- Honours
- Master of Biomedical Science

Project: Modulation of neural encoding following memory

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:

A/Prof Lucy Palmer

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science

Parish Group

Contact: Prof Clare Parish
Email: clare.parish@florey.edu.au
Location: Florey Institute, Kenneth Myer Building

Project:Can human stem cell-derived neural grafts reverse non-motor deficits in a Parkinson's Disease model?

Parkinson's disease (PD) is a progressive neurodegenerative disease. PD is caused by the loss of ventral midbrain (VM) dopamine (DA) neurons, resulting in movement disturbances. Whilst a variety of drug treatments can provide some relief to the motor symptoms of the disease, they show waning efficacy with time, are associated with various side effects and offer no long-term disease modification. In contrast, cell replacement therapy has been shown to provide long-term benefits for decades in patients. Cell transplantation involves the implantation of new dopamine neurons into the brain – either into the site of cell loss, the ventral midbrain (homotopic transplantation) or into the target tissue, the striatum in an effort to restore dopamine transmission (ectopic transplantation). Previously, transplantation has relied on the use of aborted human fetal tissue as a source of new dopamine neurons - which presents both ethical considerations and practical concerns related to tissue standardisation and availability. Advances in stem cell biology have shown that it is now possible to generate large numbers of ventral midbrain dopamine progenitors in vitro from human pluripotent stem cells (PSCs) including embryonic stem cells (ESC) and induced pluripotent stem cells (iPSC). These stem cells have the valuable attribute of proliferating, thus providing an unlimited supply.

As a laboratory we have shown that ventral midbrain dopamine progenitors derived from human pluripotent stem cells can survive transplantation, re-innervate the target striatum and correct motor dysfunction in vivo.In addition to the motor deficits (associated with dopamine loss) many PD patients also show cognitive decline. Neuroimaging studies have revealed considerable changes in gray and white matter in PD patients with cognitive impairment including cortical and hippocampal atrophy. Of relevance, just 5% of cells within our neural grafts are dopaminergic neurons, with many other neuronal populations present, and showing extensive innervation of other brain nuceli. There is little understanding of the impact this non-dopamine component has on graft or host function – whether it is detrimental or in fact of additional benefit. We therefore wish to determine whether our neural grafts can have an impact on non-motor symptoms – via dopamine and/or non-dopamine mechanisms. The proposed Honours research project will assess graft survival, composition, targeted reinnervation of brain structures, motor and cognitive changes in PD mice. Such findings could highlight the benefit of cell replacement strategies as a more 'complete' therapy, encompassing both motor and non-motor symptoms, for Parkinson's disease patients.

Project Supervisor

Prof Clare Parish

Co-Supervisor

Dr Niamh Moriarty

Project Availability

- 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
Website: go.unimelb.edu.au/wx5i
go.unimelb.edu.au/cx5i

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:

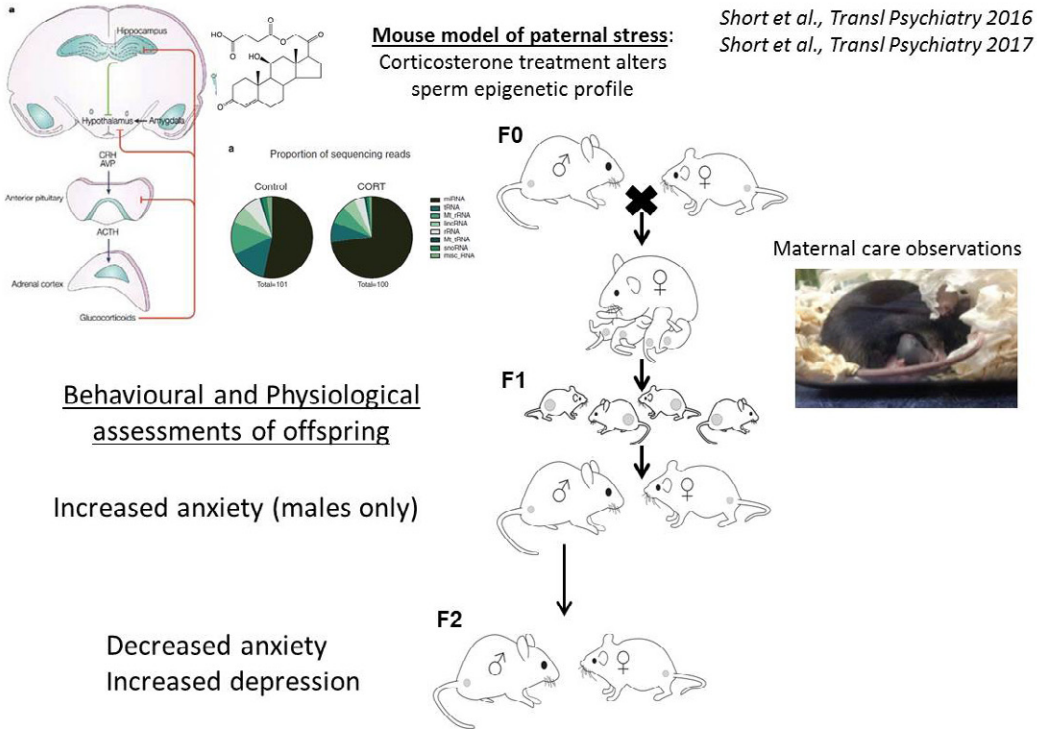
Dr Terence Pang

Project Co-supervisor:

Prof Anthony Hannan

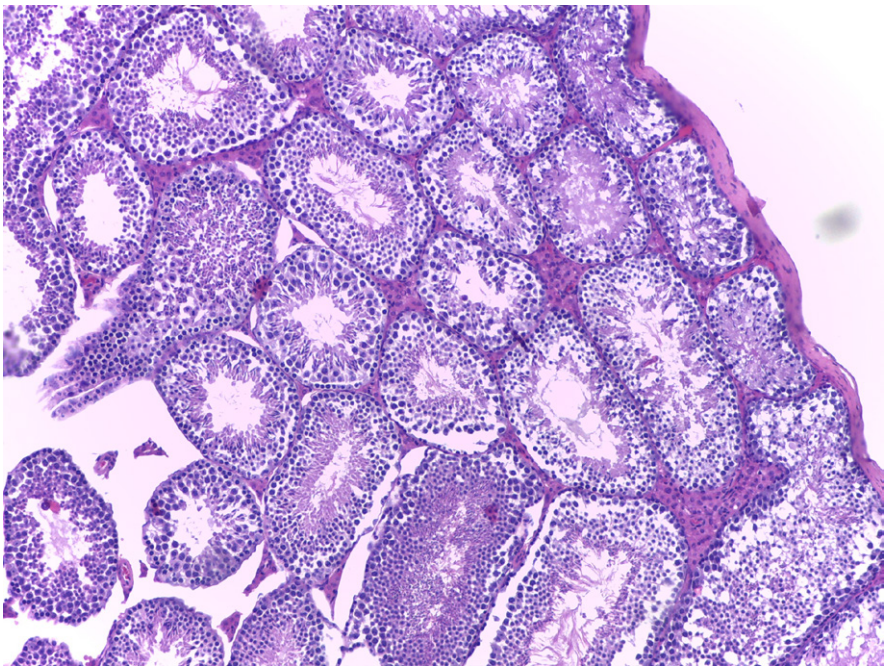
Project Availability:

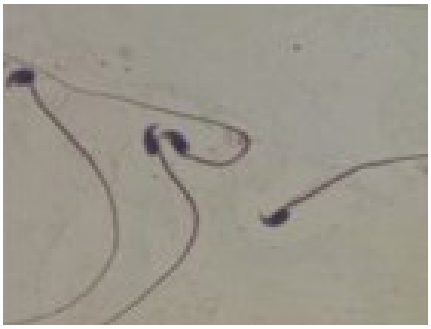
- M.Phil/PhD
- Honours
- Master of Biomedical Science

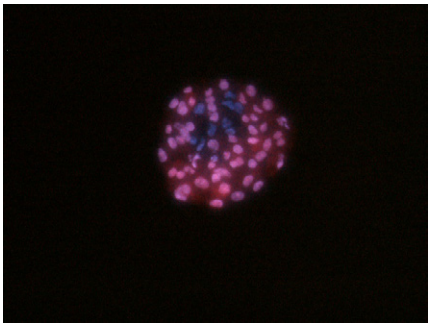


Project: How do paternal experiences impact offspring behaviour, physiology and reproductive fitness?

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)

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science

Pardoe Group

Contact: A/Prof Heath Pardoe
Email: heath.pardoe@florey.edu.au
Location: Florey Institute of Neuroscience and Mental Health

Our research group investigates the causes and consequences of epilepsy in the human brain. The primary tool we use for these investigations is Magnetic Resonance Imaging (MRI). We use MRI-based image analysis to identify brain changes in epilepsy, and assist in surgical planning for individuals with severe epilepsy. We're also interested in developing statistical techniques to assist in planning and carrying out big neuroimaging studies.

Project: Functional MRI of brain network dynamics during sustained attention

Project Description: The aim of the project is to track neural activity changes associated with sleep onset in vivo using functional MRI. Study participants underwent an extended 20 minute functional MRI acquisition with simultaneous recording of in-scanner eyetracker video. The eyetracker videos will be used to infer sleep onset during the scan and functional MRI data will be used to determine how neural activity is modified in response to these changes. This project provides an exciting and unique opportunity to map how brain-wide neural activity changes in the early stages of sleep and may provide insight into mechanisms underlying brain dysfunction in neurological disorders with sleep-related issues such as dementia and epilepsy.

Project Supervisor

A/Prof Heath Pardoe

Project Availability

- Honours

Project. Deep learning approaches for MRI-based labelling of neuroanatomical structures following epilepsy surgery

Project Description Brain surgery is an effective intervention for individuals with medically unresponsive epilepsy. The location and extent of removed brain regions predict the likelihood of postsurgical seizure freedom. The aim of this project is to train a deep learning model to label resected brain regions and other related neuroanatomical structures using a large dataset (n = 500) of postsurgical MRI scans. This project would be well suited to students with an interest in data science and artificial intelligence techniques.

Project Supervisor

A/Prof Heath Pardoe

Project Availability

- Honours

Project. Identifying disease pathogenesis of RYR1 variants

Project Description Mutations in the sarcoplasmic reticulum calcium release channel, Ryanodine receptor 1 (RYR1), result in the most common non-dystrophic congenital myopathy. Given the large size of this gene, there are a significant numbers of potentially disease-causing variants which do not reach the current threshold for definitive genetic diagnosis. Using the advantages of the zebrafish model system combined with confocal microscopy, immunofluorescence techniques and live imaging, this project will determine the pathogenicity of RYR1 variants of uncertain significance.

Project Supervisor

Dr Avnika Ruparelia

Project Availability

- Honours
- Master of Biomedical Science
- PhD

Project: MRI-based brain age prediction in epilepsy

Project Description: Over the last decade artificial intelligence methods have been developed that use brain MRI scans to predict the age of an individual. Differences between brain MRI-predicted age and chronological age have been identified in a number of neurological disorders and health conditions, suggesting that brain age is a candidate measure of overall brain health. In epilepsy, preliminary research has demonstrated that indivduals with severe epilepsy and ongoing seizures have brains that appear 4-5 years older than non-epilepsy individuals. Causative factors underlying these brain age changes remain unclear. The purpose of this study is to use brain MRI scans obtained in a large dataset of individuals with epilepsy and healthy controls to identify how brain aging varies by epilepsy subtype, and to determine how epilepsy-related health factors influence brain age. This study will assist researchers in identifying how epilepsy affects the health of our brain.

Project Supervisor

A/Prof Heath Pardoe

Project Availability

- Honours

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 andmicroscopy

Project Supervisor:

Dr Lachlan Thompson

Project Co-supervisor:

Dr Jennifer Hollands

Project Availability:

- M.Phil/PhD
- 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

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science

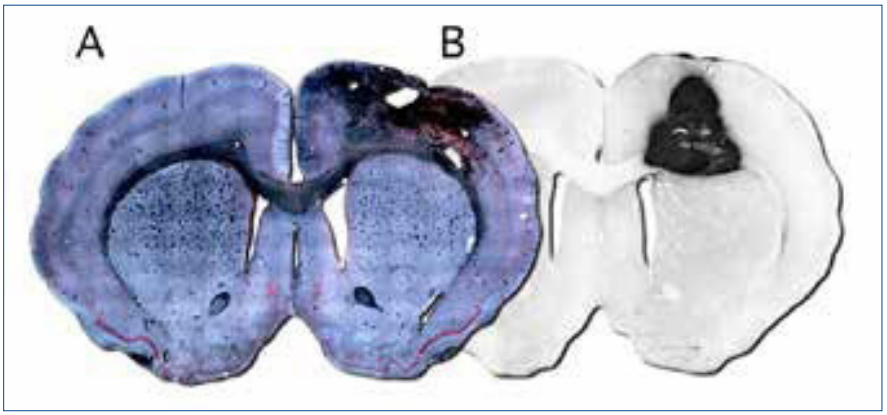


Figure. A) Damage to the cortex caused by focal ischemia. B) A stem cell derived graft of new cortical neurons to replace those lost to the ischemic damage.

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

Project Availability:

- M.Phil/PhD
- Honours
- Master of Biomedical Science

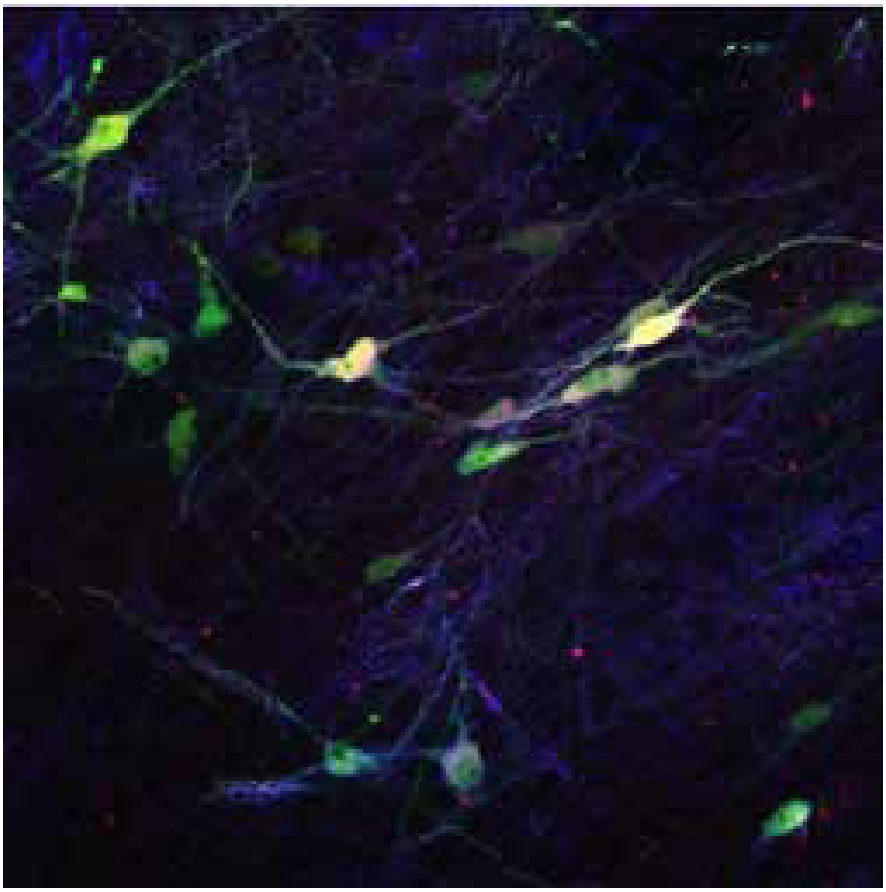


Figure: Functional midbrain dopamine neurons generated from human pluripotent stem cells

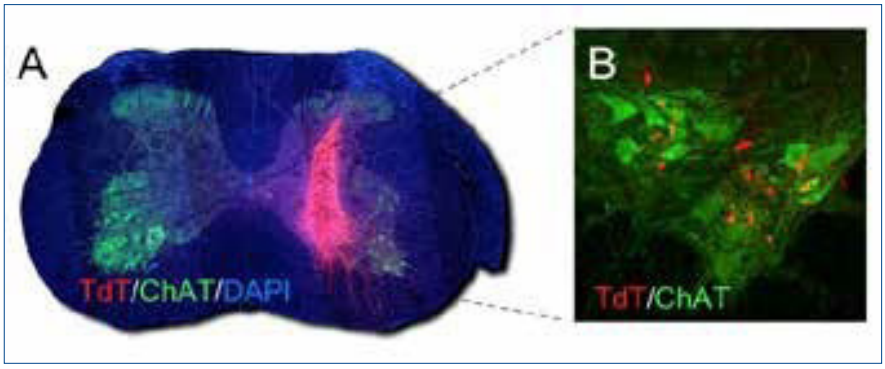


Figure. A) Graft of human stem cell derived neurons engineered to express a fluorescent protein (TdT) to allow for identification in the host brain. B) The transplanted neurons migrate to and intermingle with the diseased host motor neurons (ChAT) and may provide trophic support

Turner Group

Contact: A/Prof Bradley Turner
Email: bradley.turner@florey.edu.au
Location: Florey Institute of Neuroscience and Mental Health

Autophagy is the primary waste recycling pathway in all our cells that targets and degrades misfolded proteins, aggregates and damaged organelles. Autophagy is essential for cell survival, bioenergetics, immunity and inflammation. Waste recycling by autophagy plays a pivotal role in neurons and their supporting glial cells of the central nervous system (CNS).

Multiple lines of evidence indicate that CNS autophagy is impacted by age. For example, age-related neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and motor neuron disease (MND) all shows protein aggregate accumulation in neurons and glial cells of the CNS indicating autophagy abnormalities. Conversely, many regimes that promote longevity such as fasting elevate autophagy. Before we can modulate autophagy pathway for therapeutic purposes, an understanding of cell-specific neurotypical autophagy is essential. So far, many studies have investigated neuronal autophagy while glial autophagy remains under-explored. This project will analyse tissue from a novel transgenic autophagy reporter mouse model (RFP-EGFP-LC3) to quantify autophagy in vivo to study the effects of aging on glial autophagy dynamics. Brain and lumbar spinal cord tissue have been already collected and cryostat sectioned from adult (6 months), middle-aged (12 months) and advanced aged (18 months) transgenic autophagy reporter mice. This project will involve conducting immunohistochemistry, confocal microscopy and image analysis using computer software to quantify autophagy flux in microglia and oligodendrocytes.

The findings will reflect fundamental cell type-specific differences in autophagy pathway dynamics in the CNS and their responses to ageing to inform development of therapeutic strategies for age-related neurodegenerative diseases such as MND. Techniques: immunohistochemistry, confocal microscopy and 3D image analysis techniques (e.g. IMARIS).

Project: Investigating age-related effects of autophagy on motor neurons and glial cells

Autophagy is the main intra-cellular catabolic pathway that targets and degrades misfolded proteins, aggregates and damaged organelles. Autophagy is essential for cell survival, bioenergetics, immunity and inflammation. Waste recycling by autophagy plays a pivotal role in neurons of the central nervous system (CNS), as they do not divide and thereby cannot dilute out unwanted substances. Multiple lines of evidence indicate that CNS autophagy is impacted by age. The signature pathology of age-related neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and motor neuron disease (MND) is protein aggregate accumulation in CNS. Conversely, many regimes that promote longevity such as fasting elevate autophagy. So far, the exact role of ageing on neuronal and glial cell autophagy remains unknown due to the lack of techniques to accurately measure autophagy pathway degradation rate termed autophagy flux in vivo. This project will use a novel transgenic autophagy reporter mouse model (RFP-EGFP-LC3) that allows accurate quantification of autophagy flux in vivo to study the effects of aging on CNS autophagy pathway dynamics.

Brain and lumbar spinal cord tissue have been already collected from the adult (6 months), middle-aged (12 months) and advanced aged (18 months) transgenic RFP-EGFP-LC3 mice. This project will involve cryostat sectioning of the tissue, conducting immunofluorescence microscopy and image analysis using computer software to quantify autophagy flux in motor neurons and glial cells. The findings will reflect fundamental cell type-specific differences in autophagy pathway dynamics in the CNS and their responses to ageing to inform development of therapeutic strategies for age-related neurodegenerative diseases such as MND.

Techniques: Transgenic mouse models, histology (cryostat sectioning, immunohistochemistry), confocal microscopy and 3D image analysis techniques.

Project Supervisor:

Dr Nirma Perera

Project Co-supervisor:

A/Prof Bradley Turner

Project Availability:

- Honours
- Master of Biomedical Science

Project: Screening autophagy enhancing drugs for Motor Neuron Disease

Autophagy is the main intra-cellular catabolic pathway that targets and degrades misfolded proteins, aggregates and damaged organelles. Autophagy is essential for cell survival, bioenergetics, immunity and inflammation. Waste recycling by autophagy plays a pivotal role in neurons of the central nervous system (CNS), as they do not divide and thereby cannot dilute out unwanted substances. The signature pathology of neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and motor neuron disease (MND) is protein aggregate accumulation in the CNS. Therefore, autophagy induction offers enormous potential as an effective treatment strategy for neurodegenerative diseases. However, until recently techniques were unavailable to accurately measure the autophagy pathway degradation rate termed autophagy flux in vivo. This project will use a novel transgenic autophagy reporter mouse model that allows accurate quantification of autophagy flux in vivo to screen 8 repurposed drugs or nutraceuticals to identify the best compound/(s) that can induce autophagy flux in the CNS.

We have treated the transgenic autophagy reporter mice (RFP-EGFP-LC3) with 8 repurposed drugs or nutraceuticals and collected the brain and lumbar spinal cord tissue. This project will involve cryostat sectioning of these tissue, conducting immunofluorescence microscopy and image analysis using computer software to quantify autophagy flux in motor neurons. The findings will identify compound/(s) that can enhance autophagy flux which future studies will use as potential treatments for MND.

Techniques: Transgenic mouse models, histology (cryostat sectioning, immunohistochemistry), confocal microscopy and 3D image analysis techniques.

Project Supervisor:

Dr Nirma Perera

Project Co-supervisor:

A/Prof Bradley Turner

Project Availability:

- Honours
- Master of Biomedical Science

Project:Investigating autophagy pathway dynamics at the neuromuscular junction

Project Description. Autophagy is the primary waste recycling pathway in all our cells that targets and degrades misfolded proteins, aggregates and damaged organelles. Autophagy is essential for cell survival, bioenergetics, immunity and inflammation. Waste recycling by autophagy plays a pivotal role in highly metabolic tissue such as skeletal muscle and at the neuromuscular junction (NMJ; the chemical synapse connecting motor neurons and skeletal muscle fibres). Changes in the structure and function of NMJs are hallmarks of neurodegenerative diseases such as motor neuron disease (MND). However, the status of autophagy at the NMJ in response to aging and MND is poorly understood. Before we can modulate autophagy pathway for therapeutic purposes, an understanding of cell-specific autophagy is essential. Although many studies have investigated autophagy in tissue such as liver and kidney, autophagy dynamics at the NMJ and skeletal muscle remains under-explored. This project will analyse muscle tissue from a novel transgenic autophagy reporter mouse model (RFP-EGFP-LC3) to quantify the effects of MND and aging on muscle autophagy dynamics. Gastrocnemius and tibialis anterior muscle from MND mice as well as adult (6 months), middle-aged (12 months) and advanced aged (18 months) mice have been already collected.

This project will involve cryostat sectioning of muscle tissue, conducting immunohistochemistry, confocal microscopy and image analysis with computer software to quantify autophagy flux at the NMJ. The findings will reflect fundamental differences in autophagy pathway dynamics at the NMJ in responses to ageing and MND to inform development of therapeutic strategies. Techniques: Tissue cryostat sectioning, immunohistochemistry, confocal microscopy and 3D image analysis (e.g. IMARIS software).

Project supervisor

Dr Nirma Perera

Co-supervisor

A/Prof Bradley Turner

Project availability

- Honours

Project: Induced pluripotent stem cell-based organoid and cellular models for understanding disease mechanisms and identifying therapies for motor neuron disease

Project Description: Induced pluripotent stem cells (iPSCs) derived from those with motor neuron disease (MND) have potential to revolutionise our ability to identify effective treatments. Our research has already identified axonal degeneration phenotypes in cultures of both familial and, for the first time, sporadic MND motor neurons derived from patient-specific iPSCs. These neuronal models provide excellent tools for screening of potentially therapeutic compounds and for understanding disease pathology.

Project supervisor

Dr Duncan Crombie

Co-supervisor

A/Prof Bradley Turner

Project availability

- Honours
- Master of Biomedical Science

Walker Group

Contact: Dr Leigh Walker
Email: leigh.walker@florey.edu.au
Location: Florey Institute of Neuroscience and Mental Health

Project: The role of feeding-related hormones on alcohol use disorders

Project Description: 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. A midbrain region, Edinger-Westphal nucleus, densely expresses feeding related hormones and receptors for sex steroid hormones and neuropeptides that drive excessive alcohol consumption, yet how this region integrates peripheral information to drive behaviour is unknown. Using cutting-edge molecular and behavioural neuroscience technologies, this project aim to:

1. Map the expression of estrogen and progesterone receptors in the Edinger-Westphal of male and female mice using RNAscope and immunohistochemistry
2. Determine the impact of sex steroid hormones on neuropeptide expression and receptor expression in the Edinger-Westphal nucleus using qPCR.
3. Functionally examine the role of Estrogen receptors in the Edinger Wesphal nucleus using pharmacogenetic approaches.

Project Supervisor

Dr leigh Walker

Project Co-Supervisor:

Dr Andrew Lawrence

Project Availability

- Honours
- Master of Biomedical Science

Project: Hallucinogens to treat co-morbid stress and alcohol use disorders

Project Description: MDMA (ecstasy) and psilocybin (mushrooms) are posed to change the landscape of mental health treatment. However, how they exert their actions in the brain are not well understood. We have developed a novel rodent model to explore the role of hallucinogens in co-morbid PTSD and alcohol use disorder and identify the mechanism(s) by which the anti-anxiety and alcohol consumption behaviours occur. This project will use rodent models to understand the impact of MDMA and psilocybin in fear conditioning and extinction, and combine behavioural neuroscience, basic pharmacology and molecular biology to answer this question.

Project Supervisor

Dr leigh Walker

Project Co-Supervisor:

Dr Andrew Lawrence

Project Availability

- Honours
- Master of Biomedical Science

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