



THE UNIVERSITY OF
MELBOURNE



DEPARTMENT OF ANATOMY AND PHYSIOLOGY 2022

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](https://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 18 months 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 2022 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 2021/2022 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 Academic Services (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





METABOLIC AND CARDIOVASCULAR SCIENCES



Contact: Prof Lea Delbridge

Email: imd@unimelb.edu.au

Location: Department of Anatomy and Physiology

The Cardiac Phenomics Laboratory research is about understanding 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).

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 to understand how for women and men, cardiac ‘difference’ may be managed with optimized therapeutic tools.

Student projects in the Cardiac Phenomics lab 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 assay, confocal microscopy, microarray gene profiling, 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.

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:

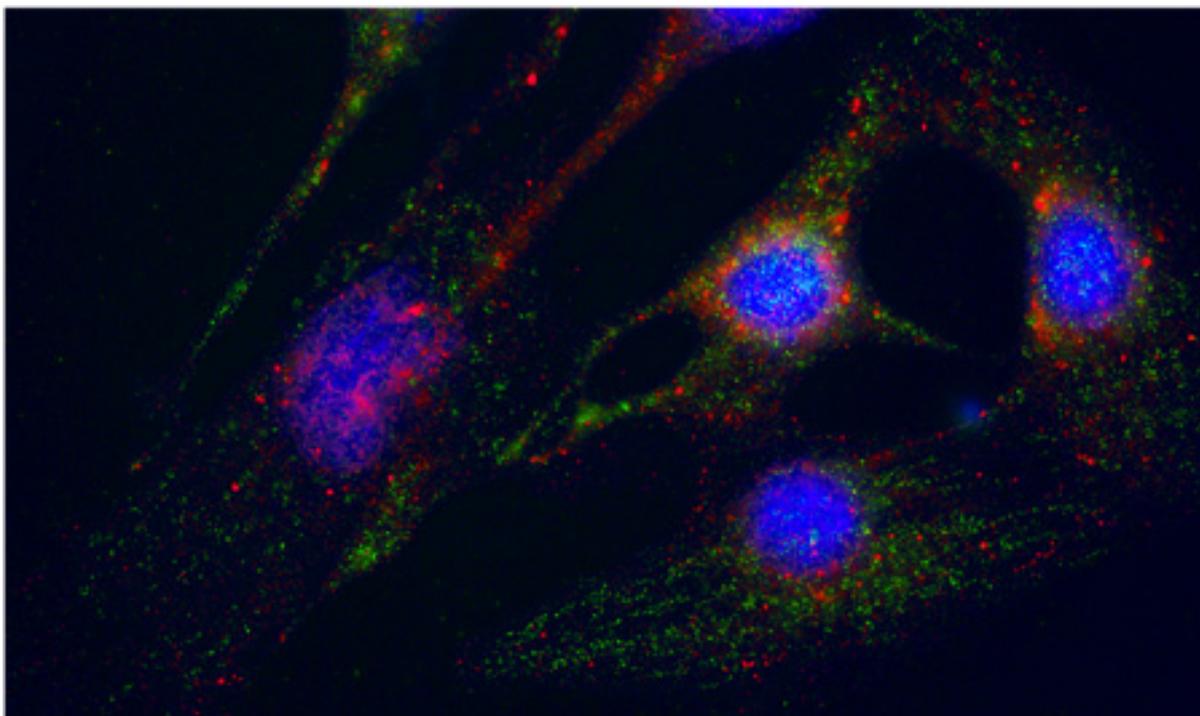
Prof Lea Delbridge

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

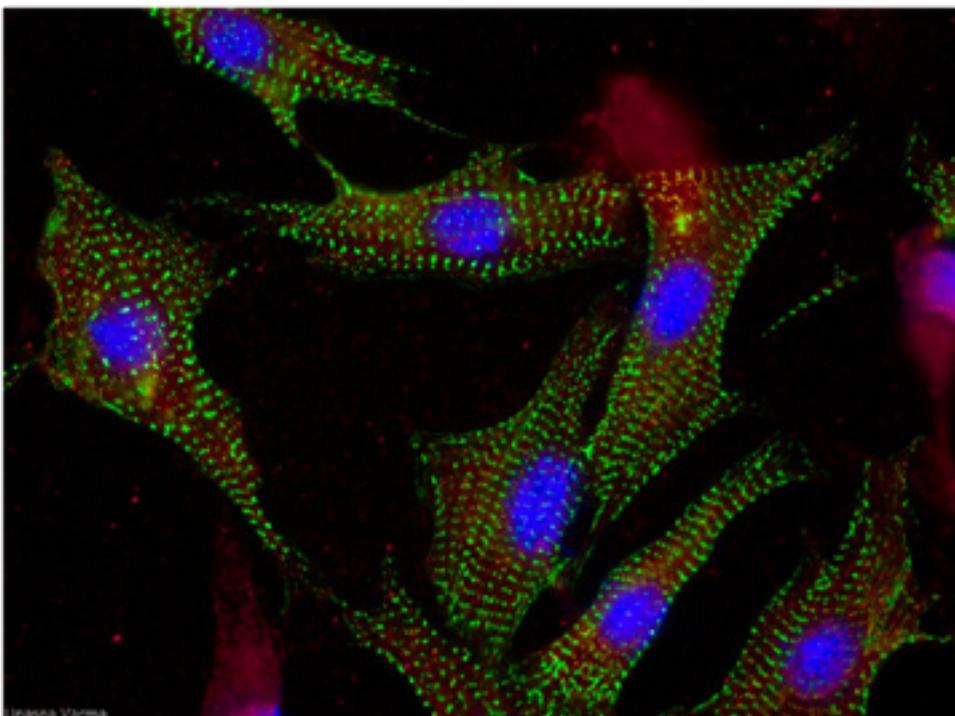
Prof Lea Delbridge

PROJECT CO-SUPERVISOR

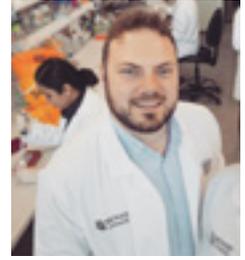
Dr Kate Weeks

PROJECT AVAILABILITY

- PhD
- Master of Biomedical Science



Project 2



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: FROM EMBRYO TO OBESITY: IDENTIFYING THE NEURONAL CIRCUITRY OF CHILDHOOD OBESITY

In a high-throughput screen we identified several proteins whose secretion was increased in the presence of NASH and we now aim to determine if these proteins affect (1) glucose metabolism and glycaemic control, (2) insulin sensitivity and (3) lipid metabolism in the key peripheral tissues of metabolism, including skeletal muscle, liver, adipose tissue and the pancreas.

PROJECT SUPERVISORS

Dr. 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. Garron Dodd

PROJECT CO-SUPERVISOR:

Dr Benjamin Parker

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 - i.e. 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 steatosis and inflammation, hepatocyte ballooning and significant fibrosis. We aim to understand what proteins a NAFLD/ NASH liver secretes and if these proteins contribute to changes in systemic metabolism (Can a fatty liver drive type 2 diabetes?).

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.

PROJECT: UNDERSTANDING THE EFFECTS OF NASH-SECRETED FACTORS ON GLUCOSE AND LIPID METABOLISM

In a high-throughput screen we identified several proteins whose secretion was increased in the presence of NASH and we now aim to determine if these proteins affect (1) glucose metabolism and glycaemic control, (2) insulin sensitivity and (3) lipid metabolism in the key peripheral tissues of metabolism, including skeletal muscle, liver, adipose tissue and the pancreas.

PROJECT SUPERVISOR:

Dr Magdalene Montgomery

PROJECT AVAILABILITY:

- Master of Biomedical Science
- Honours

PROJECT: UNDERSTANDING THE FORMATION AND SECRETION OF MITOCHONDRIA-DERIVED VESICLES

We made the novel discovery that the diabetic heart secretes mitochondrial components within vesicles as a means to dispose of damaged proteins and lipids. This project will assess the endocrine (i.e. secretory) function of the heart, with a focus on the formation and secretion of such mitochondria-derived vesicles (MDV). In addition, this project will investigate the systemic metabolic impact of these MDV in peripheral tissues.

PROJECT SUPERVISOR:

Dr Magdalene Montgomery

PROJECT CO-SUPERVISOR:

Dr Paula Miotto

PROJECT AVAILABILITY:

- PhD
- Honours



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





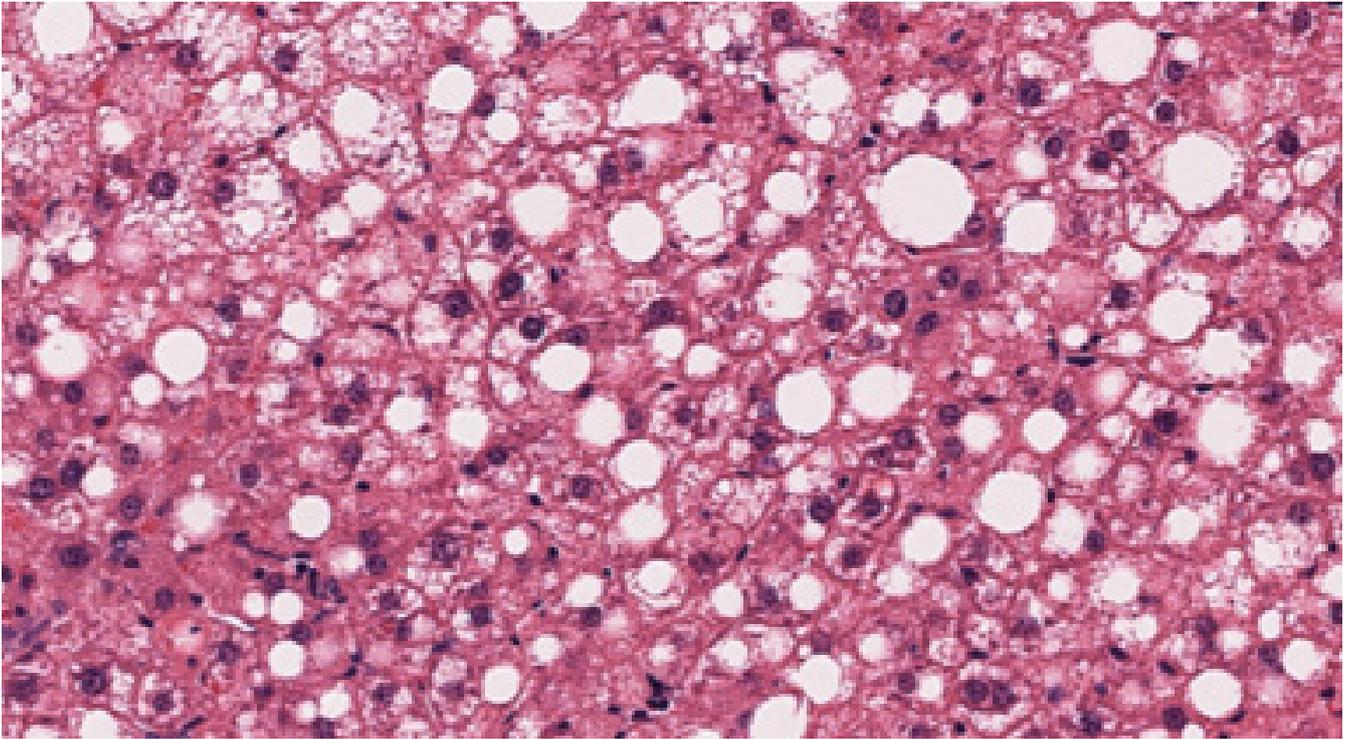


Image showing liver section from a patient with fatty liver disease. Note the abundance of lipid droplets (white circles).

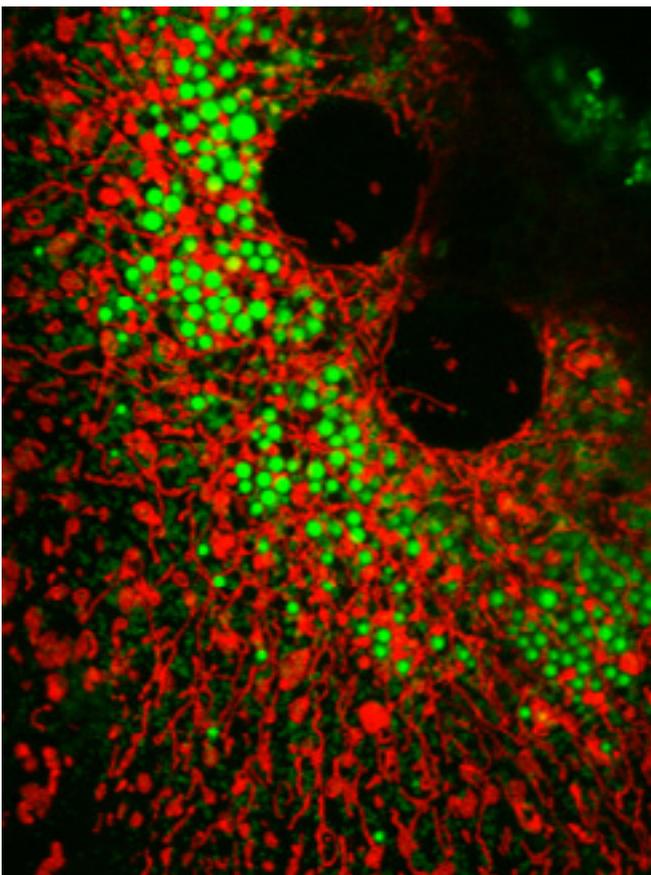


Image showing lipid droplets (green) in close association with mitochondria (red) in liver cells.

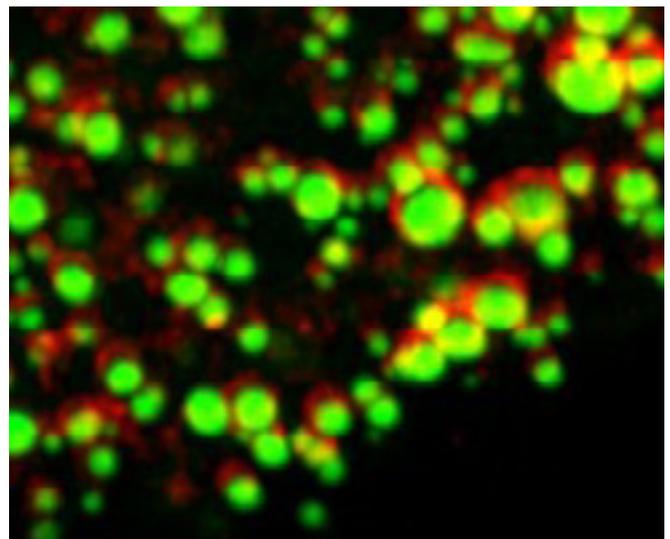


Image of lipid droplets (green) within liver cells in close contact with a protein that regulates lipid metabolism (red).



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

Dr. Rene Koopman

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

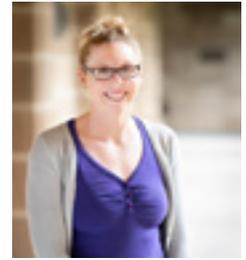
PROJECT CO-SUPERVISOR:

Dr Rene Koopman

PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science
 - Honours

BASIC & CLINICAL MYOLOGY



Contact: Dr Kate Murphy

Email: ktmurphy@unimelb.edu.au

Location: Department of Anatomy and Physiology

PROJECT: INVESTIGATING THE ROLE OF CACHEXIA IN THE RESPONSE TO SURGICAL TUMOUR RESECTION IN MICE

Cancer cachexia is the progressive skeletal muscle wasting and weakness observed in 80% of cancer patients. Cachexia reduces mobility and quality of life and in the most severe cases, can lead to death. Unfortunately, there are currently no effective treatments for cachexia, with one of the reasons being a lack of understanding of the cellular mechanisms responsible for this profound wasting and weakness. Chemotherapy and surgical interventions exist only to address primary tumour burden and the efficacy of both are dramatically limited by cachexia itself. This project will use cell- and animal-based experiments to comprehensively identify how skeletal muscle responds to chemotherapy and surgical tumour resection and will lead to developing more targeted therapies to address cancer associated muscle wasting.

PROJECT SUPERVISOR:

Dr Kate Murphy

PROJECT CO-SUPERVISOR:

Prof Gordon Lynch

A/Prof Paul Gregorevic

PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science
- Honours

PROJECT: MUSCLE WASTING IN MULTIPLE SYSTEM ATROPHY

Atypical Parkinson's includes neurological disorders where patients exhibit some clinical features of Parkinson's Disease (PD) but have additional symptoms not typically present in PD. One of the most common forms of atypical Parkinson's is multiple system atrophy (MSA), a rare, fatal neurodegenerative disease with mean survival of only 7-9 years following symptom onset. Motor impairments are one of the most debilitating aspects of MSA and a primary contributor is muscle wasting which robs patients of their strength and capacity to perform daily tasks and live independently. In the worst cases, failure of the breathing muscles and/or heart can lead to death.

A therapy to combat the muscle wasting and weakness in MSA is needed urgently. This project will use animal-based experiments to comprehensively characterise the muscle wasting in a mouse model of MSA and to test the therapeutic potential of promising treatments to combat the muscle wasting and weakness exhibited by MSA mice. The findings will be critical to devising ways that can enhance the mobility, independence, and quality of life of patients with MSA and related conditions.

PROJECT SUPERVISOR

Dr Kate Murphy

PROJECT CO-SUPERVISOR

Dr David Finkenstein

Prof Gordon Lynch

PROJECT AVAILABILITY

- PhD
- Master of Biomedical Science
- Honours

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

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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

CLINICAL NUTRITION AND MUSCLE METABOLISM



Contact: Dr Rene Koopman

Email: rkoopman@unimelb.edu.au

Location: Department of Anatomy and Physiology

PROJECT: CHARACTERISING THE PATHWAYS RESPONSIBLE FOR ICU-ACQUIRED WEAKNESS

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:

Dr. Rene Koopman

PROJECT CO-SUPERVISOR:

Prof. Gordon Lynch

PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science
- Honours

PROJECT: ESTABLISH THE EFFECT OF GLYCINE/SERINE METABOLISM ON SKELETAL MUSCLE CELL GROWTH

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:

Dr. Rene Koopman

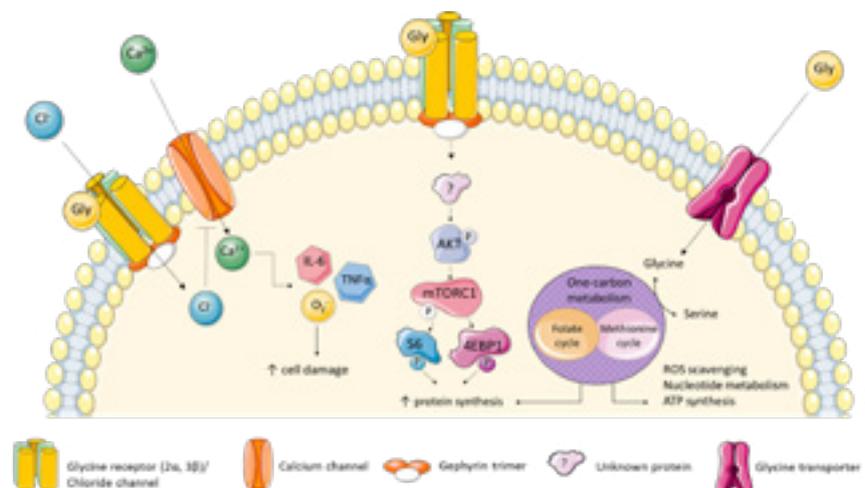
PROJECT CO-SUPERVISOR:

Dr. Marissa Caldwell

Prof. Gordon Lynch

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: 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 TGF β SIGNALLING NETWORK AS A CAUSE OF SKELETAL MUSCLE DISORDERS, AND A TARGET FOR NEW MUSCLE THERAPEUTICS.

The Transforming Growth Factor β (TGF β) 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 TGF β network in skeletal muscle and determine how unique components of the TGF β 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

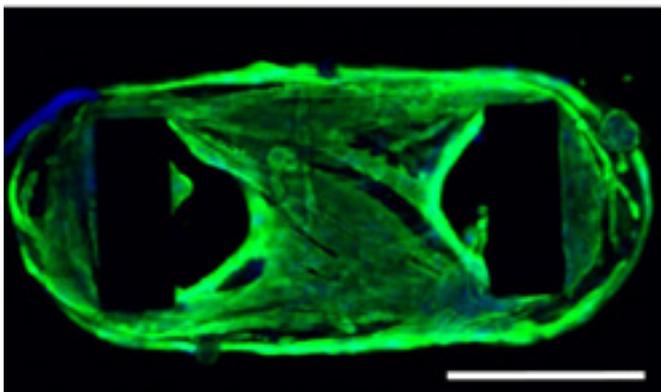
PROJECT CO-SUPERVISOR:

Dr. Rachel Thomson

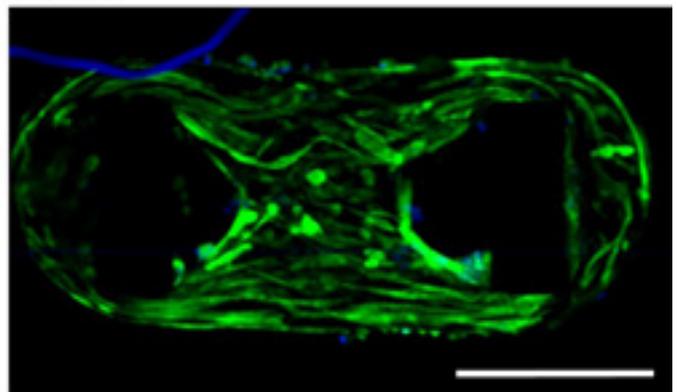
PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science
- Honours

DNA TITIN



AAV:TET/MCS



AAV:TET/DUX4

MUSCLE RESEARCH AND THERAPEUTICS



Contact: Dr Kevin Watt

Email: kevin.watt@unimelb.edu.au

Location: Department of Anatomy and Physiology

PROJECT: THE HIPPO PATHWAY IN SKELETAL MUSCLE

We have demonstrated essential roles for a protein called YAP in skeletal muscle differentiation, growth and metabolism (Watt et al 2010, 2015, 2021). Recently, new small molecules that can target YAP have been developed. This project will use human muscle fibre culture models to assess the functional consequences and potential therapeutic benefit of these compounds.

PROJECT SUPERVISOR:

Dr. Kevin Watt

PROJECT CO-SUPERVISOR:

A/Prof Paul Gregorevic

PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science
- Honours

PROJECT: SINGLE-MOLECULE IMAGING OF TRANSCRIPTION FACTORS IN SKELETAL MUSCLE

This project will use new single-molecule, super-resolution imaging techniques to study the behaviour of critical transcription factors in human and mouse skeletal muscle fibres providing new insight into the mechanisms that control skeletal muscle biology.

PROJECT SUPERVISOR:

Dr. Kevin Watt

PROJECT CO-SUPERVISOR:

A/Prof Paul Gregorevic

PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science
- Honours



SENSORY NEUROSCIENCE

FLETCHER GROUP



Contact: Prof Erica Fletcher

Email: elf@unimelb.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

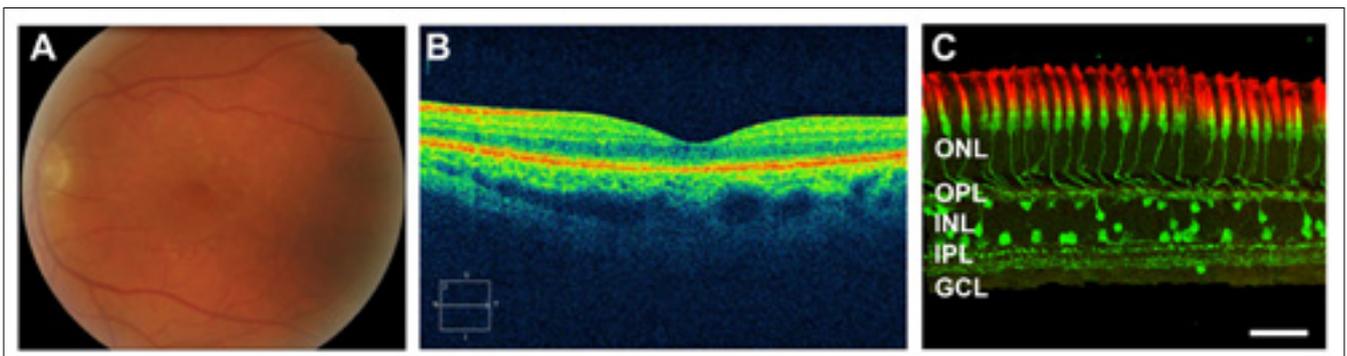
PROJECT CO-SUPERVISOR:

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.



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. A δ 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 handling, 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



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:

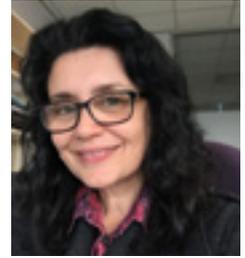
Dr Alice McGovern

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 PREMATURETY 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

A photograph of two scientists in a laboratory setting. In the foreground, a woman with dark hair tied back, wearing a white lab coat and blue gloves, is smiling as she uses a pipette to transfer liquid into a petri dish. In the background, a man with glasses, also in a white lab coat and blue gloves, is looking down at the work. On the table, there is a rack of several test tubes containing liquids of various colors (blue, green, red, brown). The entire image has a light blue tint.

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

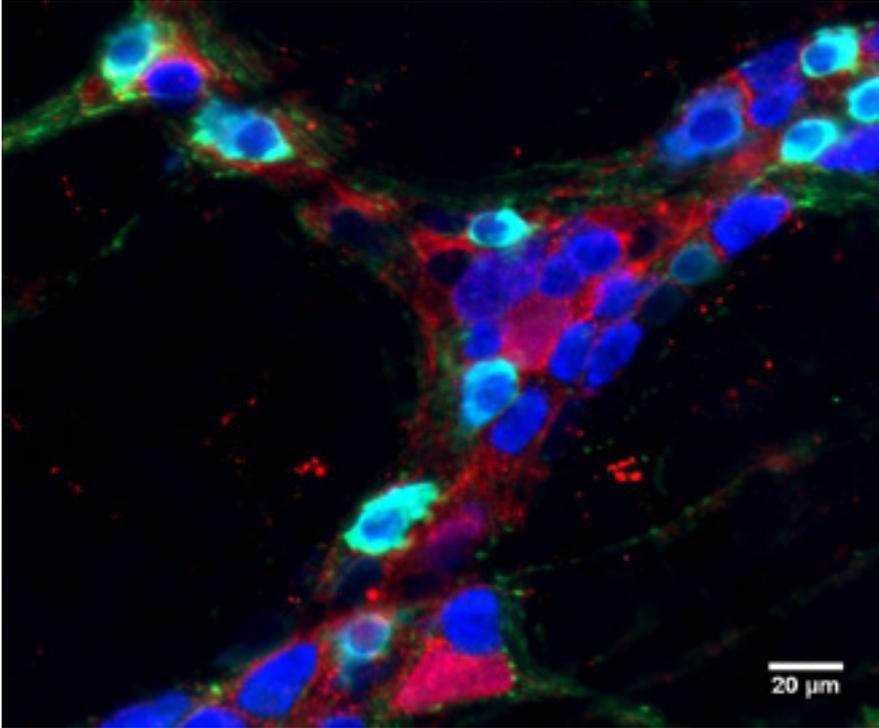
PROJECT CO-SUPERVISOR:

Prof Joel Bornstein

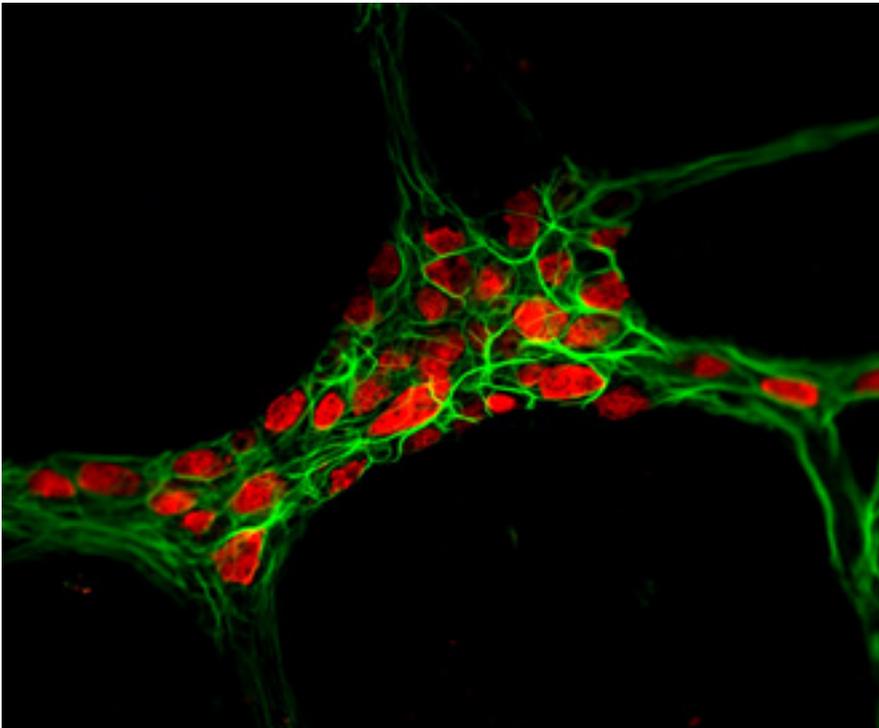
PROJECT AVAILABILITY:

- 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 DISEASE GENE CHARACTERISATION WITH NANOPORE SEQUENCING

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

in order to translate genetic findings into a better understanding of disease pathology and identify potential treatment targets. The opportunity exists to perform the sequencing and/or conduct analysis of the expression data and would suit students interested in either laboratory work or computational analysis.

PROJECT SUPERVISOR:

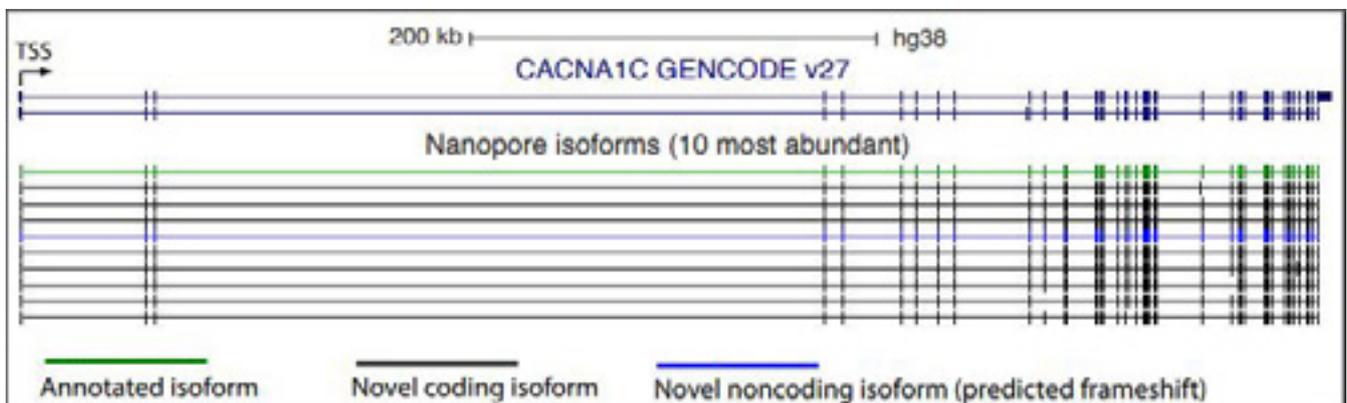
Dr Michael Clark

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: THE ROLE OF GENE ISOFORMS IN HUMAN BRAIN DEVELOPMENT

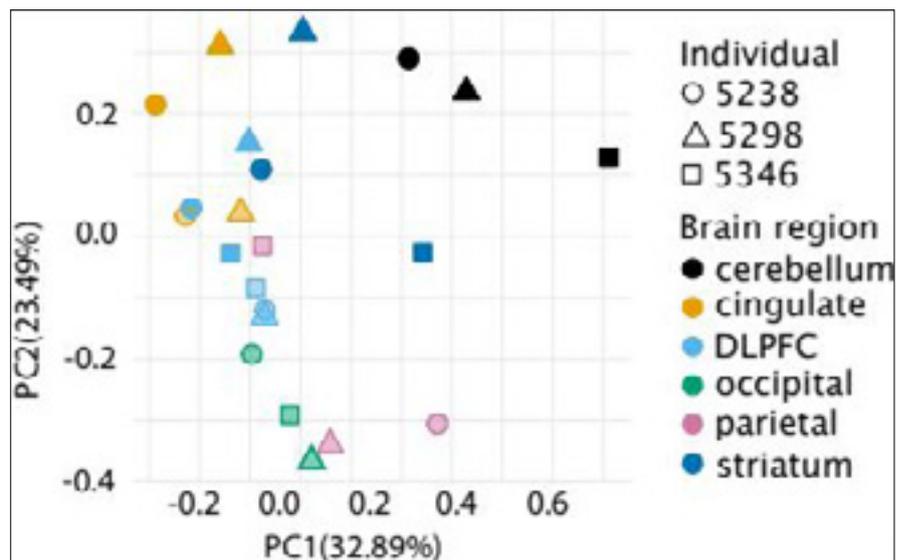
Human brain development is an exquisitely complex process, which is tightly controlled by networks of gene products. Almost all human genes make multiple mRNA products (known as isoforms), but current technologies lack the ability to identify and functional characterise the repertoire of gene isoforms controlling brain development. This project will profile gene isoforms in developing neurons using single cell long-read Nanopore sequencing, a ground-breaking new technique for characterising isoform expression in individual cells. To examine gene isoforms in the developing brain stem cells will be differentiated 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 the stem cell differentiations and sequencing and/or bioinformatic analysis of expression data for this project and would suit students interested in either laboratory work or computational analysis.

PROJECT SUPERVISOR:

Dr Michael Clark

PROJECT AVAILABILITY:

- Honours
- Master of Biomedical Science



CANCA1C expression variation between human brain regions.



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 treating bowel diseases through neuromodulation, an exciting new approach in which nerves are stimulated to treat disordered function, through drug development and by unravelling the basic mechanisms essential for digestive health. We are also working to understand the reasons why gastrointestinal functions become disordered when there are pathologies of the central nervous system, such as in Parkinson's Disease.

PROJECT: NEURO-IMMUNE INTERACTIONS: NERVE PATHWAYS CONTROLLING INFLAMMATION IN THE INTESTINE

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

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

PROJECT SUPERVISOR:

Dr Martin Stebbing

PROJECT CO-SUPERVISOR:

Prof John B Furness

PROJECT AVAILABILITY:

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

PROJECT: NOVEL DRUGS AND RECEPTORS FOR TARGETING NEURAL CONTROL OF DIGESTIVE FUNCTION

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

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

PROJECT SUPERVISOR:

Dr Ruslan Pustovit

PROJECT CO-SUPERVISORS

Prof John B Furness

PROJECT AVAILABILITY:

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

PROJECT: BRAIN-GUT AXIS: NEURAL PATHWAYS CONTROLLING THE STOMACH AND THEIR RELEVANCE FOR TREATMENT OF GASTROPARESIS

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

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

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

PROJECT SUPERVISORS

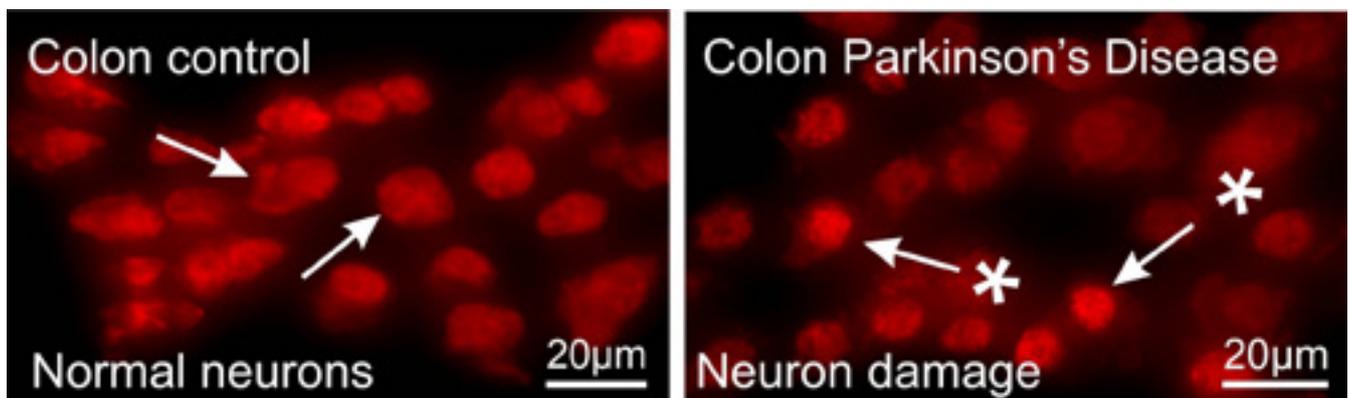
Prof John B Furness

PROJECT CO-SUPERVISORS

Dr. Martin Stebbing

PROJECT AVAILABILITY:

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



Damage to neurons in the gut wall in an animal model of Parkinson's Disease

PROJECT: A STEM CELL THERAPY TO REVERSE THE EFFECTS OF SPINAL CORD INJURY

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

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

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

PROJECT SUPERVISORS

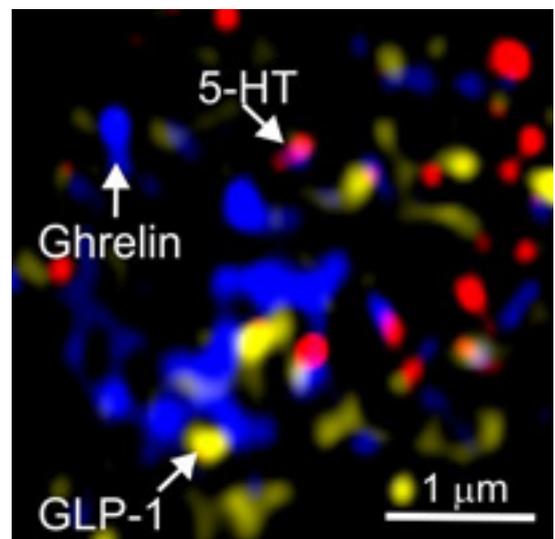
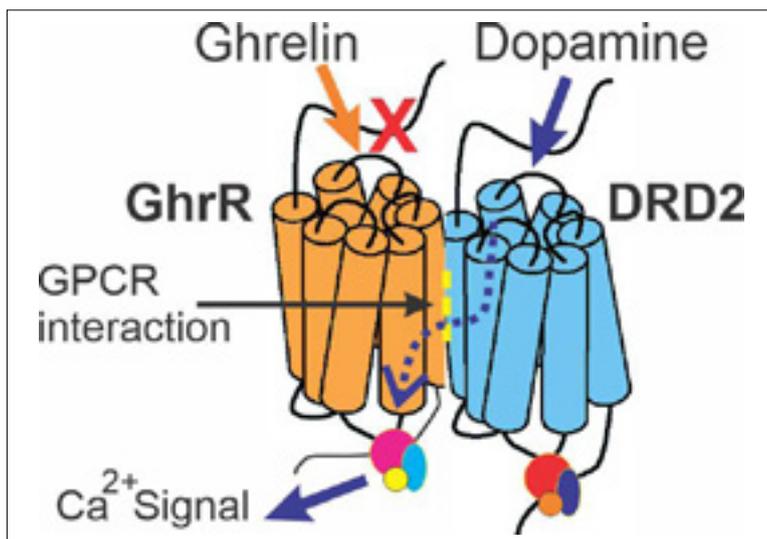
Prof John B Furness

PROJECT CO-SUPERVISORS

Dr Lincon Stamp

PROJECT AVAILABILITY:

- M.Phil/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



Contact: Dr Jenny Gunnensen

Email: jenny.gunnensen@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 Gunnensen

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 Gunnensen

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 Gunnensen

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.

This includes studies to provide high resolution maps and computational models of these neural circuits in rodents and human specimens, define how these peripheral, spinal and brain circuits develop; and how they might be manipulated to provide clinical treatments in diverse medical specialties including urology, gastroenterology, sexual medicine, neurology and pain medicine. We are supported by the US National Institutes of Health (NIH) SPARC program and have also contributed to the NIH-funded GenitoUrinary Development Molecular Anatomy Project database (GUDMAP).

PROJECT: 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:

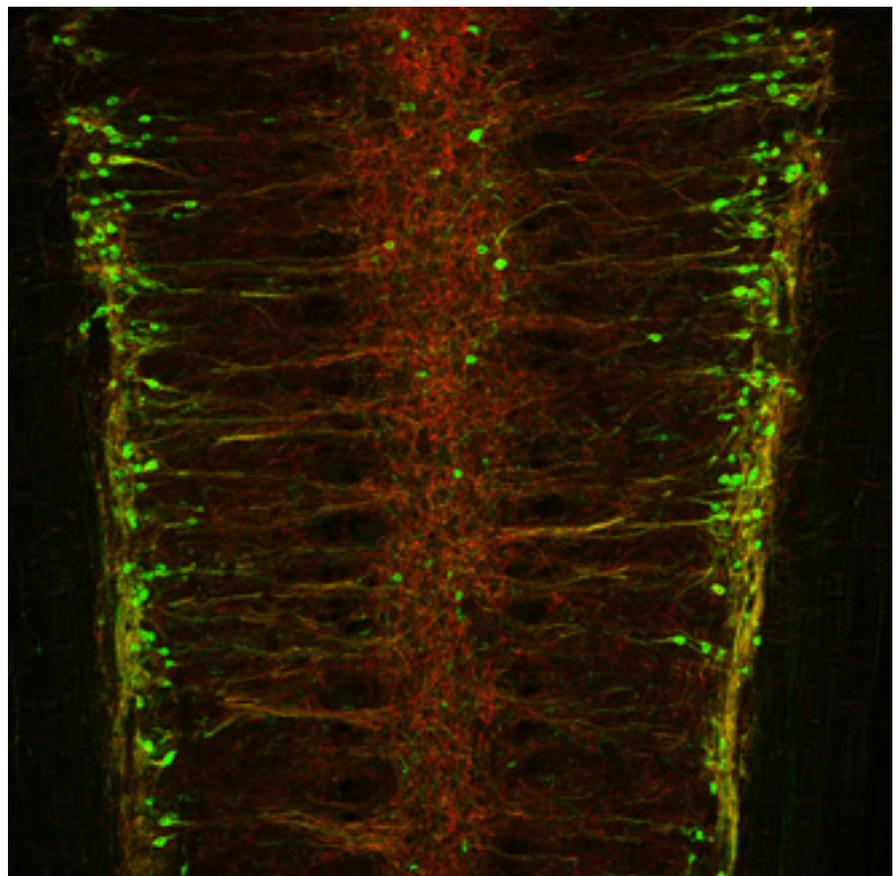
Prof Janet Keast

PROJECT CO-SUPERVISOR:

Dr Peregrine Osborne

PROJECT AVAILABILITY:

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



PROJECT: DEVELOPMENT OF AUTONOMIC AND NOCICEPTIVE NERVE CIRCUITS

A range of studies are available in this area and are especially suited to students with a strong background in developmental biology or neural structures. Urogenital function is regulated by autonomic neurons in the pelvic ganglia (known as the inferior hypogastric plexus in people) and sensory neurons in lumbosacral dorsal root ganglia. In comparison to other parts of the autonomic nervous system, the pelvic ganglia are very unusual. For example, they are very different in males and females, and they continue to be very sensitive to actions of steroids, even in adults. Most unusually, they are mixed sympathetic-parasympathetic ganglia, leading to questions of how these ganglia develop, and how their connections with two different regions of the spinal cord (lumbar and sacral) are determined correctly when they first form. Very little is known about how this part of the autonomic nervous system develops and what initiates its sexual dimorphism. These are critical to understanding developmental abnormalities and may also point to mechanisms that can be activated in adults to repair axons after injury. Other projects are available to investigate the unique features of developing sacral nociceptive neurons that are later involved in sexually dimorphic pelvic pain conditions.

PROJECT SUPERVISORS:

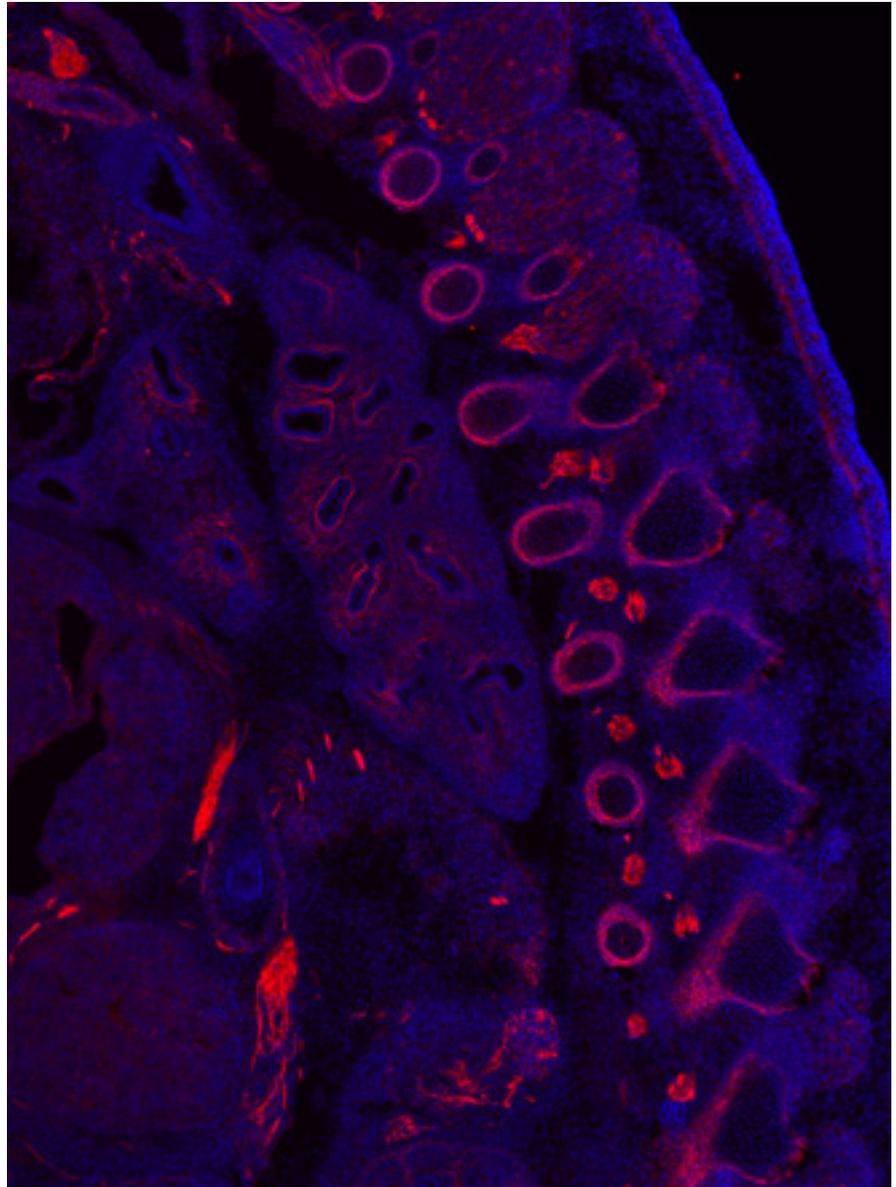
Prof Janet Keast

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 plexus 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:

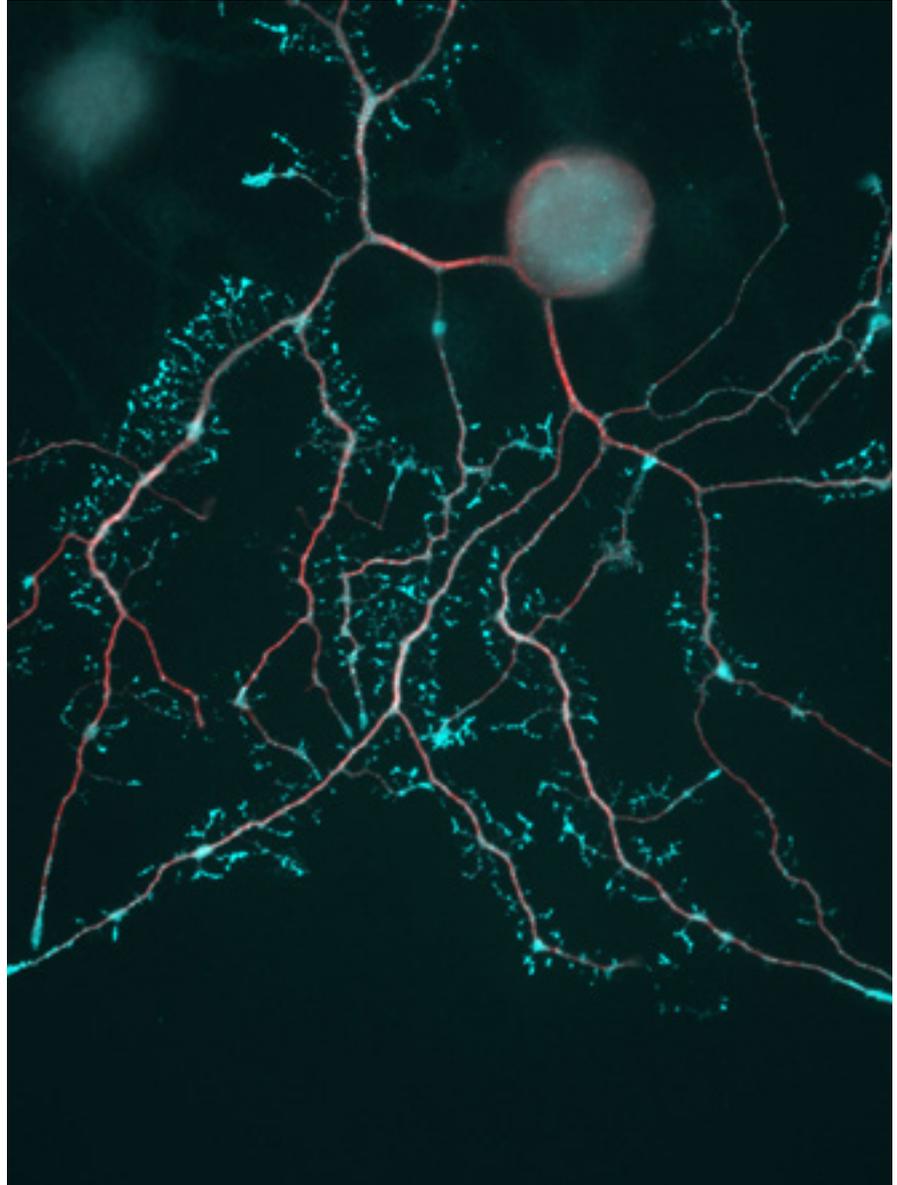
Prof Janet Keast

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:

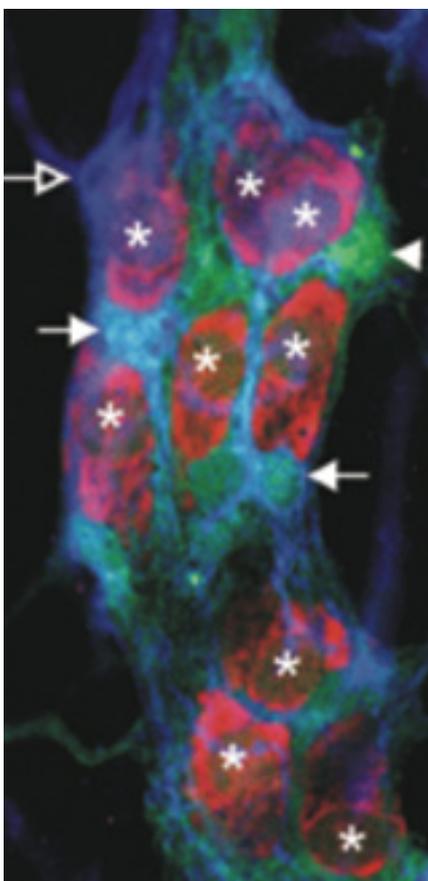
Prof Christine Wells

Dr Jarny Choi

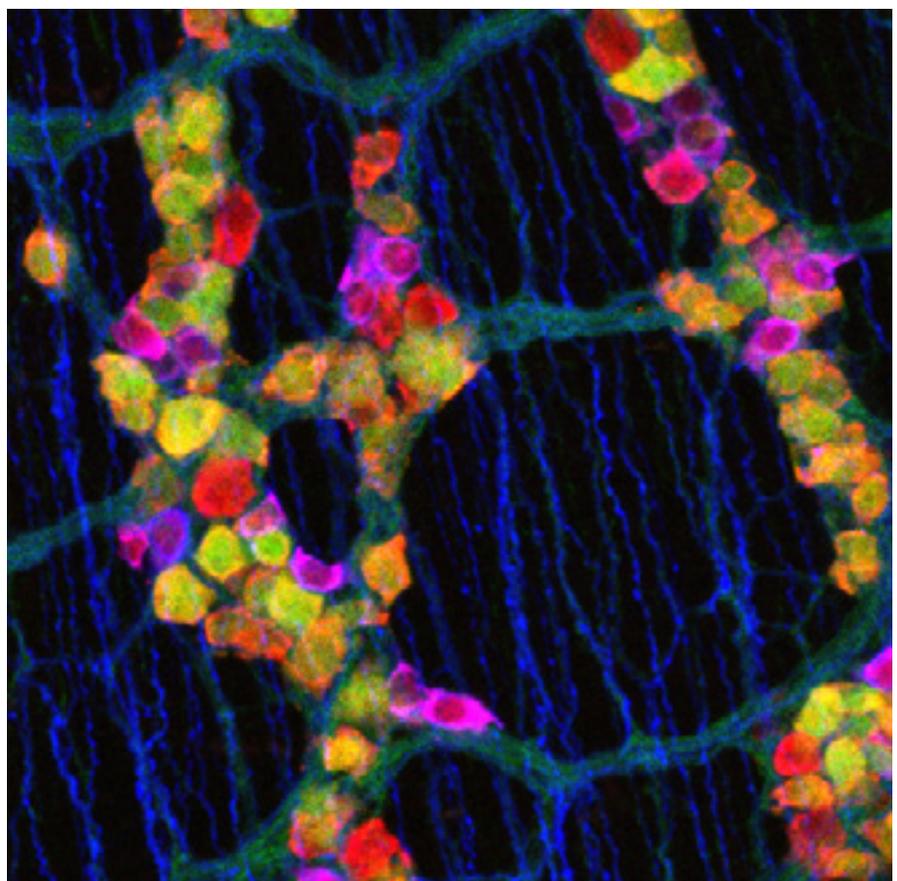
Dr Lincon Stamp

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.



Contact: Dr Song Yao

Email: song.yao@florey.edu.au

Location: Department of Anatomy and Physiology

The Neurovascular Biology

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: TRPV1 CHANNEL ACTIVATION LEADING TO INCREASED METABOLIC ACTIVITY, THERMOGENESIS AND DECREASED BGL. HOW?

We have shown that either TRPV1 channels activation or adenosine receptor antagonism both activate brown adipose tissue (BAT) thermogenesis (anti-obesity) and reduce BGL (anti-diabetic) in humans. We have recently shown that adenosine receptor located in the CNS are sufficient to activate BAT, the precise Location: and mechanism for TRPV1 is unknown.

PROJECT SUPERVISOR:

Dr Song Yao

PROJECT CO-SUPERVISOR:

Dr Yossi Rathner

PROJECT AVAILABILITY:

- Honours

PROJECT: CENTRAL CARDIOVASCULAR CONTROL: DOES MCP-1 ACT ON AREA POSTREMA NEURONS TO INCREASES IN BLOOD PRESSURE?

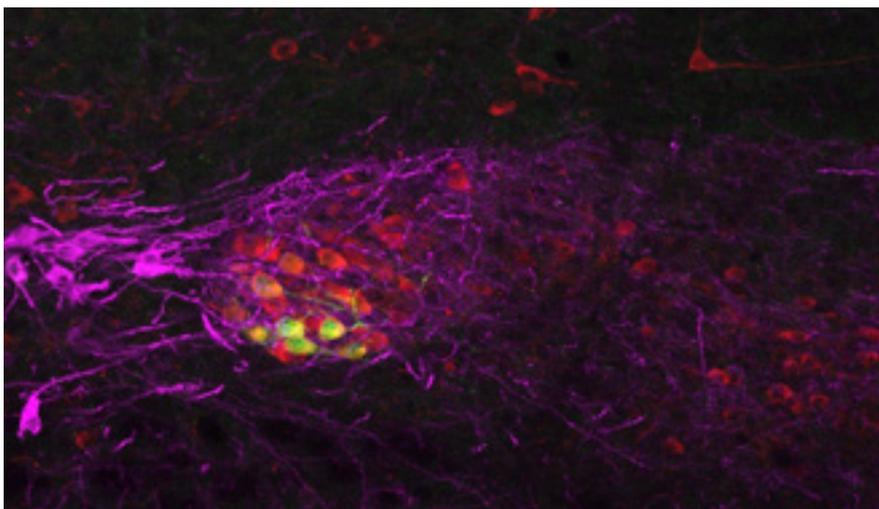
The area postrema is a circumventricular organ located in the brain stem. Because it lacks a blood-brain barrier the area postrema is exposed to a wide range of factors found in the circulation. There is much evidence to suggest that inflammatory cytokines are increased in a number of cardiovascular diseases such as hypertension and heart failure. However, the cardiovascular effect of these cytokines when exogenously applied to the area postrema is not currently known. This project will investigate the effects of the monocyte chemoattractant protein-1 (MCP-1), within the area postrema. Plasma levels of MCP-1 has been previously shown to be increased in hypertension when administered centrally (via intracerebroventricular cannula) but whether it acts within the area postrema is not known. The successful completion of the project will increase our understanding of the role of cytokines in driving changes in blood pressure at the level of the area postrema and how this signaling might be altered in disease states such as hypertension.

PROJECT SUPERVISOR:

Dr Song Yao

PROJECT AVAILABILITY:

- Honours



A photograph of a laboratory setting with a blue tint. In the foreground, a rack of multi-colored microcentrifuge tubes sits on a metal stand. A scientist in a white lab coat is visible in the background, working at a bench. The text 'STEM CELL AND DEVELOPMENTAL BIOLOGY' is overlaid in white on the left side of the image.

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: ANALYSING THE ROLE OF TRANSCRIPTIONAL REGULATORS IN DROSOPHILA STEM CELLS

We have shown that transcriptional regulators of epithelial to mesenchymal transition are required in diverse stem cell populations. This role has been conserved through evolution of animals as these proteins can be found in stem cells from *Drosophila* to humans. This project involves using CRISPR and genetically modified *Drosophila* to identify how these proteins regulate stem cell numbers and control the production of differentiated progeny cells.

PROJECT SUPERVISOR:

Prof Gary Hime

PROJECT CO-SUPERVISOR:

A/Prof Helen Abud (Monash University)

PROJECT AVAILABILITY:

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

PROJECT: IDENTIFICATION OF NOVEL REGULATORS OF STEM CELL DIFFERENTIATION

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

PROJECT SUPERVISOR:

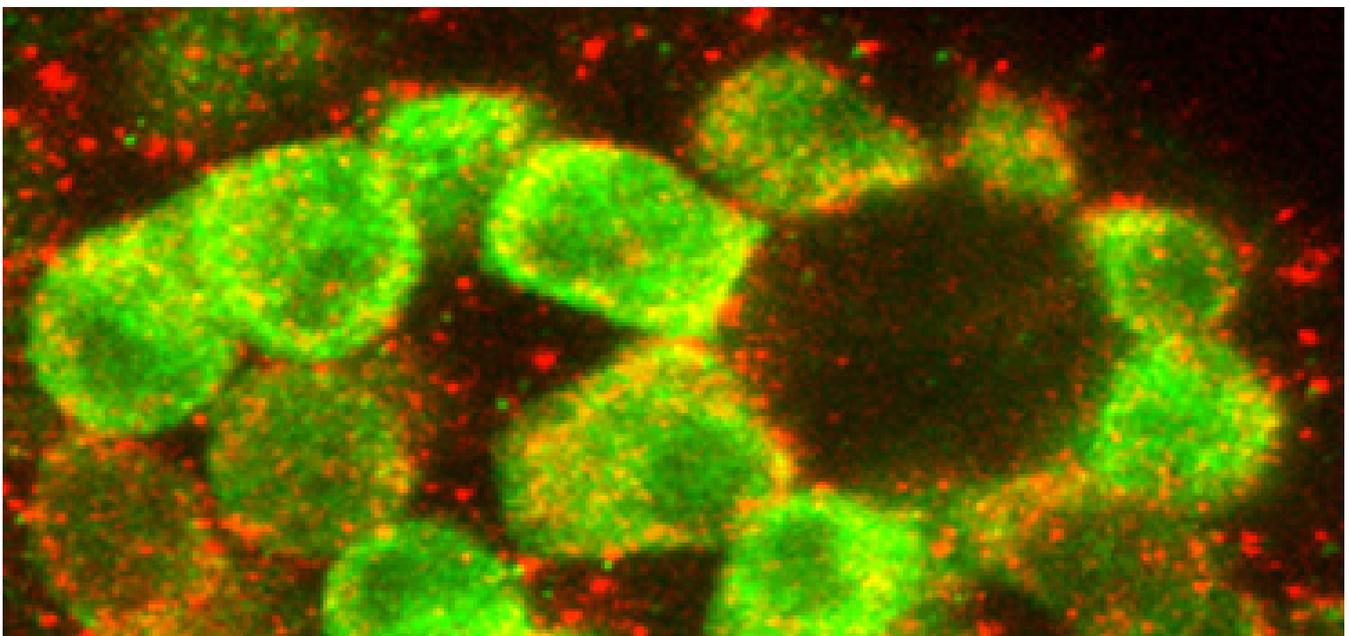
Prof Gary Hime

PROJECT CO-SUPERVISOR:

Dr Nicole Siddall

PROJECT AVAILABILITY:

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



PROJECT: HOW DOES ALTERNATIVE SPLICING REGULATE STEM CELL MAINTENANCE

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

PROJECT SUPERVISOR:

Prof Gary Hime

PROJECT CO-SUPERVISOR:

Dr Nicole Siddall

PROJECT AVAILABILITY:

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

PROJECT: DROSOPHILA MODELS OF HUMAN DISEASE

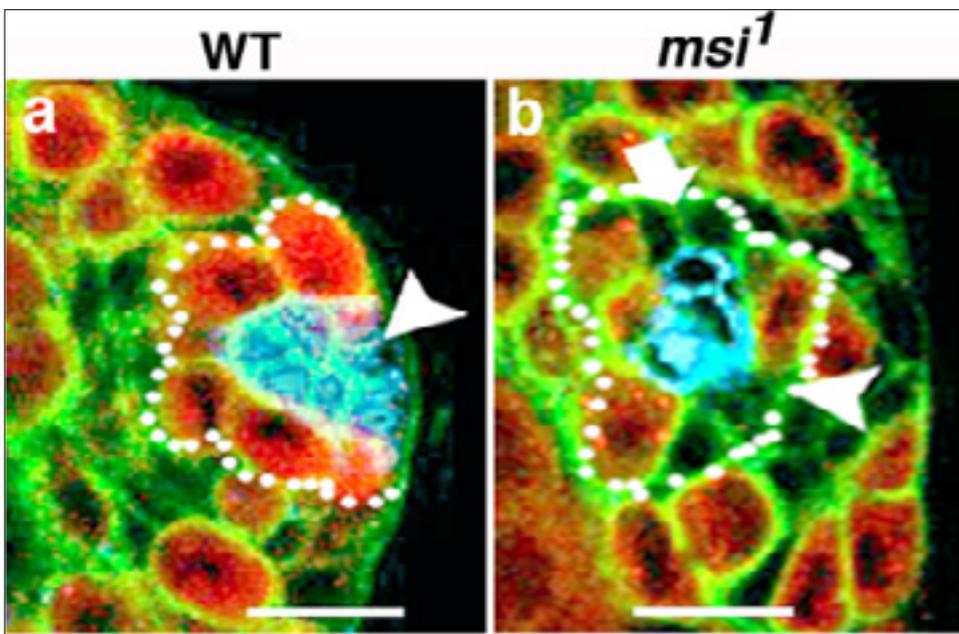
The rapid advances in sequencing of human genomes has identified many variant gene sequences that may be associated with genetic diseases. It can be difficult to unambiguously associate genetic variants with phenotypes without a direct assay. We are using *Drosophila* to model the effects of genetic 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: TRANSGENERATIONAL MODIFICATION OF SURVIVAL EFFICACY IN THE ADVENT OF CLIMATE CHANGE

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

PROJECT SUPERVISOR:

Prof Gary Hime

PROJECT CO-SUPERVISOR:

Dr Terence Pang (Florey)

PROJECT AVAILABILITY:

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

KEY PUBLICATIONS:

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

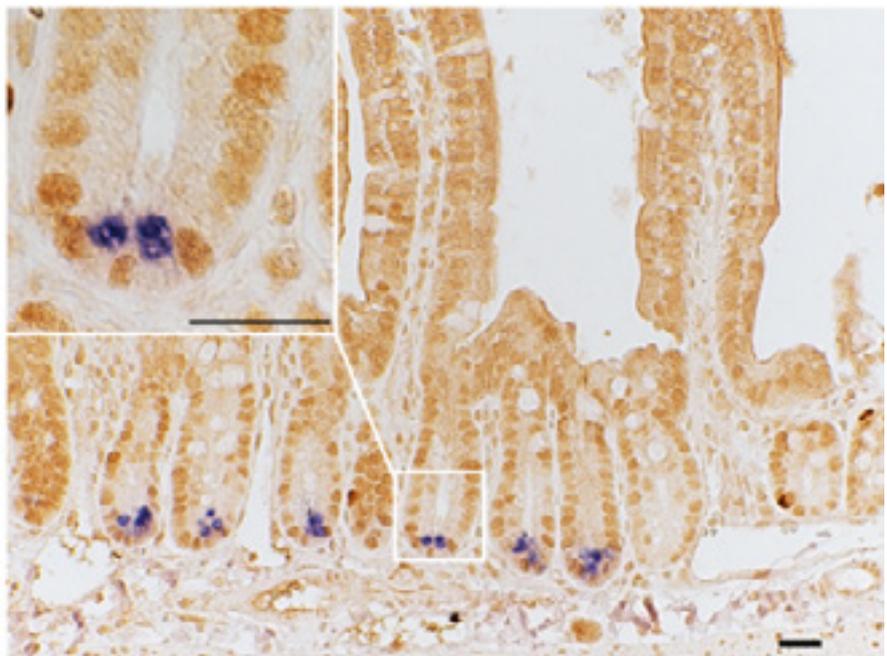
Horvay K, Jarde T, Casagrande F, Perreau VM, Haigh K, Nefzger CM, Akhtar R, Gridley T, Bex G, Haigh JJ, Barker N, Polo JM, Hime GR* and Abud HE* (2015) Snai1 regulates cell lineage **alLocation:** and stem cell maintenance in the mouse intestinal epithelium. *EMBO Journal*, * joint senior authors, 34(10):1319-35

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

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

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

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





Contact: A/Prof Enzo Porello

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Front line 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: MODELLING HYPERTROPHIC CARDIOMYOPATHY MUTATIONS IN PLURIPOTENT STEM CELLS.

Hypertrophic cardiomyopathy is the most common cause of genetic heart disease, affecting up to 39 million people worldwide. This disease causes an abnormal growth of the muscular walls of the heart and limits its capacity to fill with blood during diastole. Patients diagnosed with hypertrophic cardiomyopathy have increased risk of heart failure and sudden death. Genes that encode for contractile proteins are most frequently mutated in hypertrophic cardiomyopathy. The motor protein, myosin, responsible for the force generation of the heart is a particularly common cause. While much is known about disease due to mutations in the head region of myosin, it is unclear how mutation in the neck region cause disease. In this project, the student will investigate three myosin mutations in this neck region which have been linked to hypertrophic cardiomyopathy.

This will be performed using state-of-the-art genetic editing (CRISPR-Cas9) in human pluripotent stem cells and cardiac muscle differentiation protocols. The phenotype of these mutant heart muscle cells will be compared to control cells using confocal microscopy (cell size and organisation), as well as biochemical (ATPase assays and Western blotting), transcriptional (qPCR and RNAseq), and proteomic approaches. Additionally, comprehensive physiological phenotyping will be undertaken to measure force and calcium dynamics in both cardiac organoids (tissue level) and single myofibrils. The results of these studies will provide new information on the molecular basis of hypertrophic cardiomyopathy which could be exploited to develop novel therapies.

PROJECT SUPERVISOR

A/Prof Enzo Porello

PROJECT CO-SUPERVISOR

A/Prof David Elliott

Dr James McNamara

PROJECT AVAILABILITY

- PhD
- Honours
- Master of Biomedical Science

PROJECT: CREATING A SAFE-HARBOUR FOR HEART-SPECIFIC TRANSGENES IN PLURIPOTENT STEM CELLS.

Genetic manipulation of DNA is a key methodology in biomedical research, used in a range of approaches including fate mapping, therapeutic targeting, and disease modelling. One of the leading forms of genetic manipulation is the creation of transgenic overexpression models. In these models, the expression of a recombinant gene is regulated by a promoter sequence which determines when and where that gene will be expressed. While these models have been invaluable, they have several pitfalls. Firstly, these transgenes randomly insert into the host genome, potentially affecting the regulation of other key genes. Secondly, the regulatory promoters are prone to allow "leaky" expression of the gene in other cell types. Thirdly, many transgenes are prone to silencing upon cell differentiation and maturation. Thus, the aim of this student project is to create a "safe-harbour" for gene overexpression in heart muscle cells without the need of a promoter. This student project will test multiple regions of the genome which are transcriptionally active in heart muscle cells.

They will use CRISPR-Cas9 to edit pluripotent stem cells and create fluorescent reporters in these regions. These stem cells will be differentiated into multiple cell type to determine the specificity towards heart muscle cells. The student will use transcriptional and proteomic approaches to determine whether the safe-harbour transgene affects expression of genes and proteins important for heart function. Finally, gene mutations associated with cardiac disease will be expressed using the best safe-harbour. The effects of these mutations on heart muscle cell function will be assessed by high-speed microscopy to measure sarcomere contractility. The results of this study will provide a novel tool for cardiovascular research and disease modelling.

PROJECT SUPERVISOR

A/Prof Enzo Porello

PROJECT CO-SUPERVISOR

A/Prof David Elliott
Dr James McNamara

PROJECT AVAILABILITY

- PhD
- Honours
- Master of Biomedical Science

PROJECT: ENHANCING THE MATURATION OF PLURIPOTENT STEM CELL-DERIVED HEART TISSUE.

Pluripotent stem cells have great potential for use in regenerative medicine, disease modelling, and drug discovery due to their ability to differentiate into any cell type. However, despite significant progress in the field of stem cell biology and tissue engineering, complete maturation of stem cell-derived cardiac cells to a fully fledged 'adult' state has yet to be accomplished. To address this significant limitation for in vitro modelling, this project aims to control the maturation status of stem cell-derived cardiac cells by identifying developmentally regulated transcription factors that drive this foetal to adult switch and leveraging them to stimulate maturation in cardiac cells in vitro. This project offers the opportunity to learn a wide variety of molecular biology techniques, including Chromatin immunoprecipitation (ChIP), Western blotting, subcloning and bacterial transformant.

PROJECT: ENHANCING THE REGENERATIVE POTENTIAL OF THE HEART IN DILATED CARDIOMYOPATHY.

Dilated cardiomyopathy (DCM) is the most common cause of heart failure in children and the most common indication for heart transplantation worldwide. Despite DCM being so prevalent, there are no therapies that can regenerate damaged heart muscle cells and restore heart function in patients with DCM. Although considerable effort has gone into the development of regenerative therapies for ischaemic heart disease (i.e. myocardial infarction) in adults, very few studies have evaluated the potential of regenerative strategies in children with non-ischaemic cardiomyopathies such as DCM. As such, there is an urgent need to develop novel regenerative approaches to repair the hearts of children with DCM. This student project builds on a unique repertoire of human cardiac tissue samples and induced pluripotent stem cell (iPSC) lines available to our team through the recently established Melbourne Children's Heart Tissue Bank and innovative technologies developed by our team for differentiation of iPSCs into human cardiac organoids. We will use these state-of-the-art technologies to interrogate the mechanisms contributing to cardiomyocyte loss in DCM and determine whether induction of cardiomyocyte proliferation can restore heart function in DCM for the first time. These fundamental proof-of-concept studies will lay the groundwork for a completely new approach to heart regeneration in children with DCM, thus providing a completely novel and much needed advance in the clinical management of this condition.

PROJECT SUPERVISOR

A/Prof Enzo Porello

PROJECT CO-SUPERVISOR

A/Prof David Elliott
Dr Elizabeth Stout

PROJECT AVAILABILITY

- PhD
- Honours
- Master of Biomedical Science





SMITH GROUP



Contact: A/Prof Kelly Smith

Email: kelly.smith1@unimelb.edu.au

Location: Department of Anatomy and Physiology

The focus of the Smith group is to identify the genetic and cellular processes that regulate heart development. The heart develops by differentiating and integrating multiple tissue types via a specific sequence of events to generate the stereotypical structure of the 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 the genes in this program, 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 particularly important projects, we translate our discoveries to the 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: INVESTIGATION OF NOVEL ZEBRAFISH CARDIAC MORPHOGENESIS MUTANTS

To identify genes required for cardiac development, the lab has undertaken a forward genetic screen in zebrafish and screened for mutants with cardiac defects. This process involved mutagenizing animals, inbreeding to isolate recessive mutants with inherited heart abnormalities and mapping the causative mutation, identifying which genes are important for cardiac development. From this screen, we have identified several novel mutants and the affected genes are either completely novel or have not been previously implicated in heart development. The project will involve characterising the nature of the cardiac defect, the timing of the onset of the heart defect and may involve one or more of the following: determining the genetic pathway the gene functions in, which tissue the gene is expressed in, which cellular compartments are disrupted in mutants and whether the phenotype/s can be rescued by modification of downstream components.

PROJECT SUPERVISOR:

A/Prof Kelly Smith

PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science
- Honours



Project 1

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 of 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 generated 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: DYSREGULATION OF CARDIAC CONDUCTION AND ITS EFFECT ON THE CELLULAR LANDSCAPE OF THE MAMMALIAN HEART

A rhythmic heartbeat is essential for survival. The cardiac conduction system (CCS) is a specialised network of electrical tissue distributed throughout the heart, carrying electrical signals to control the timing of heart contraction. This occurs in tandem with cardiomyocytes in the myocardium, which cannot spontaneously beat, but are electrically competent. The coordinated beating of the heart relies on electrical currents being established and propagated, via junctions between cells and pores within cells. Any defects that affect the capacity of the CCS or myocardium to initiate or propagate these electrical currents, can result in cardiac arrhythmia. Our lab identified a novel gene, *tmem161b*, as part of a genetic screen in zebrafish and mutation of *tmem161b* has been shown to cause abnormal electrical conduction of the heart. Importantly, preliminary data establishes a similar requirement for *Tmem161b* in the mouse. We hypothesise that loss of *Tmem161b* will cause a change in the cellular landscape of the heart, impacting ion transport across cells and consequently, cardiac conduction. In this project we will use *in vivo* and *in vitro* methodologies to investigate how this important new regulator functions at the cellular and sub-cellular level, by assessing the availability, localization and distribution of macromolecules involved in ion transport (such as ion channels and gap junctions), and examine its effects on the cytoskeletal network, focal adhesions and the extracellular matrix. Methods used in this project will include genetic crosses, mouse embryology and microdissection, electron microscopy and image analysis, cell culture, transfection using plasmid constructs, immunofluorescence, confocal microscopy and analysis.

PROJECT SUPERVISOR:

A/Prof Kelly Smith

Project Co supervisor:

Dr Swati Iyer

PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science
- Honours

PROJECT: FORMATION OF THE TRABECULAR LAYER DURING CARDIAC DEVELOPMENT

The heart is the first functional organ of the body and has developed multiple specialisations to achieve efficient function during our continued lifespan. One such specialisation is the formation of the trabecular network – myocardial protrusions towards the lumen of the ventricles. They arise during embryonic stages and contribute to different aspects of heart development, including the formation of the conduction system. Despite its importance for cardiac morphogenesis, not much is known about how trabeculae emergence is controlled. Our lab has developed a transgenic tool which allows to visualize the emerging trabecular cardiomyocytes in vivo in the zebrafish heart. We developed additional genetic and transgenic models which will allow us to characterize the formation of the trabecular network and what are the mechanisms controlling the emergence of trabecular cardiomyocytes. 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, RNA synthesis), phenotypic screening by bright-field and fluorescence microscopy, confocal microscopy, image analysis and data quantification.

PROJECT SUPERVISOR:

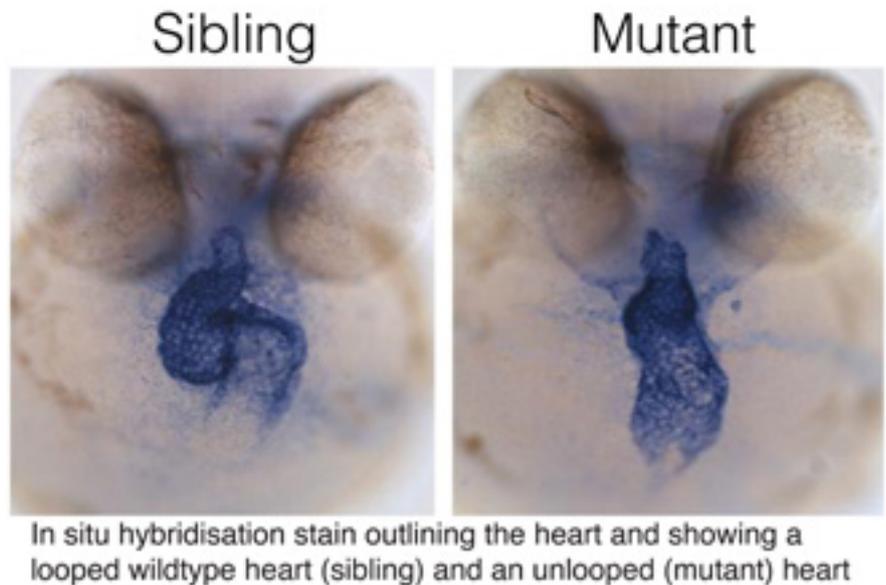
A/Prof Kelly Smith

Project Co supervisor:

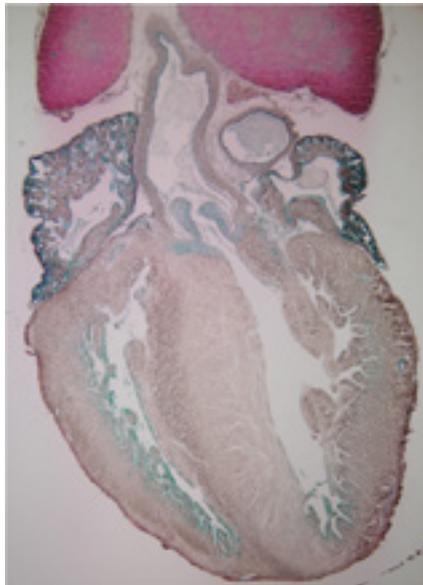
Dr Veronica Uribe-Sokolov

PROJECT AVAILABILITY:

- PhD
- Master of Biomedical Science
- Honours



Project 2



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

Project 3



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:

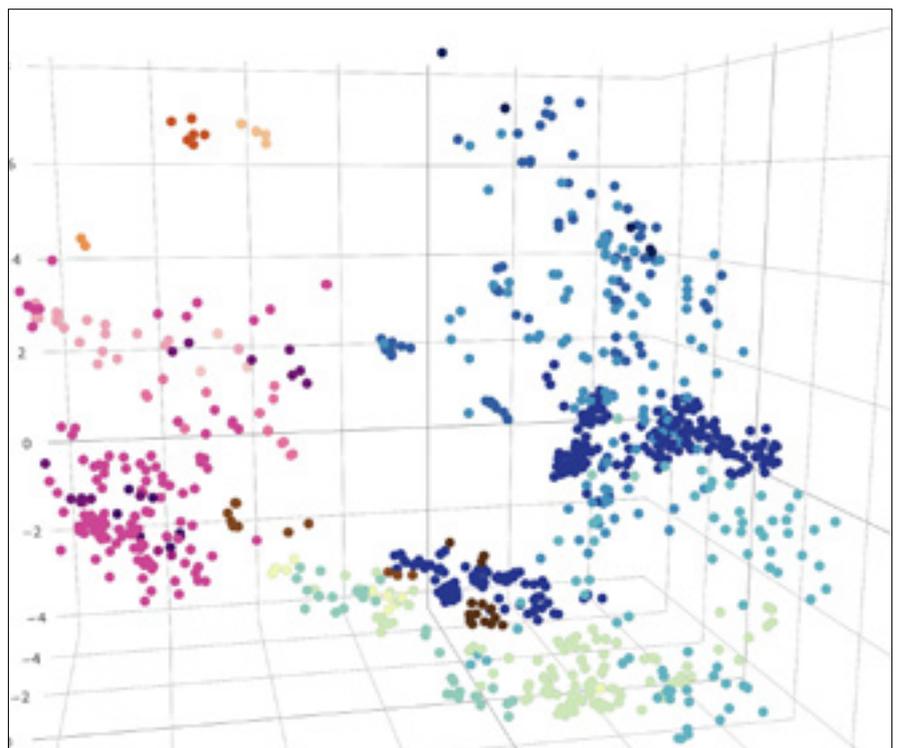
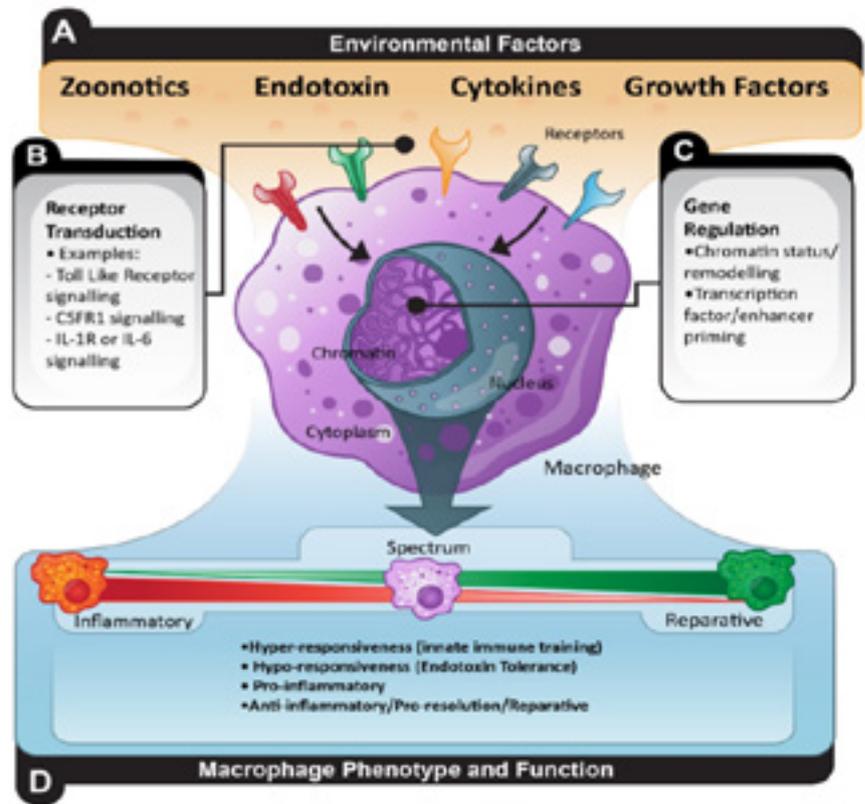
Prof Christine Wells

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 insights 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

PROJECT: THE EFFECT OF ENDOCRINE DISRUPTORS ON THE DEVELOPMENT OF THE RETE TESTIS AND EFFERENT DUCTS.

The development of the rete testis and the efferent ducts are not well described today. They form an important part of the male reproductive system and disturbance of their development will result in male infertility. Recent years has seen an increase in environmental endocrine disruptors which have been shown to affect the development of other parts of the reproductive system, but nothing is known about their influence on the rete testis and efferent duct.

PROJECT SUPERVISOR:

A/Prof Dagmar Wilhelm

PROJECT CO-SUPERVISOR

Dr Daniel Bird

PROJECT AVAILABILITY

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



MELBOURNE ACADEMY OF SURGICAL ANATOMY



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.

PROJECT: CLINICAL ANATOMY OF THE TRAPEZIUM AND ITS SOFT TISSUE CONNECTIONS

The precise anatomy of the trapezium and its soft tissue connections is poorly understood. Issues with inconsistent terminology hinder progress, but the lack of specialist anatomical studies that clearly and reproducibly document the tissue relations is most critical. This project will utilise dissection, microdissection, 3D modelling, macro-sections and medical imaging to provide a multi-model analysis of the key soft tissue structures at the base of the thumb. These data will provide a better appreciation of the muscular and ligamentous anatomy of the thumb to inform its surgical reconstruction, and clearer understanding of the stabilising relationships and how their failure contributes to degenerative joint disease of the thumb.

PROJECT SUPERVISOR

A/Prof Quentin Fogg

PROJECT AVAILABILITY

- Honours

PROJECT: CLINICAL ANATOMY OF THE TRIQUETRUM AND ITS ARTICULAR RELATIONS

The triquetrum forms an essential centre of the ulnocarpal complex. This is, perhaps, the least understood anatomical region of the human wrist, yet is implicated in high percentage of wrist dysfunction. Key to understanding this area more clearly is categorisation of the triquetrum into morphological subtypes and then understanding the variable articular and soft tissue relations for each group. The project will utilise dissection, microdissection, 3D modelling, macro-sections and medical imaging to provide a multi-model analysis of the triquetrum and its relations. These data will help provide an anatomic rationale for variable patterns of normal carpal motion, and provide a better understanding of the anatomical basis for ulnar-sided degenerative joint disease and related motion disorders.

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 Physiology. The education research group within 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:

Dr Charles Sevigny

PROJECT CO-SUPERVISOR:

Dr Angelina Fong

Dr Joseph Rathner

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 Seigny

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: Dr 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.

In STEM disciplines, hands-on small group learning activities are essential for students to develop authentic real-world skills that are sought after by employers. These 'practical classes' are highly valued by students and, moreover, provide an indispensable opportunity for students to apply and consolidate their scientific learning, teamworking skills, and to develop scientific reasoning. A practical laboratory manual is a critical teaching resource to facilitate student learning, but manuals can vary wildly between scientific disciplines. What makes a practical manual an effective resource in the first place is still not understood, nor investigated. This project seeks to define core foundational principles for the design of effective teaching resources for hands-on practical teaching sessions.

PROJECT SUPERVISOR:

Dr 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:

Dr Michelle Rank

PROJECT CO-SUPERVISOR

A/Prof Karena Waller

Dr Elisa Bone

PROJECT AVAILABILITY

- PhD
- Master of Biomedical Science

A photograph of a laboratory setting. A person wearing a white lab coat and blue nitrile gloves is holding a petri dish containing a white, foamy substance. The background is slightly blurred, showing laboratory equipment and shelves with various containers. The overall color palette is dominated by white, blue, and light grey.

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

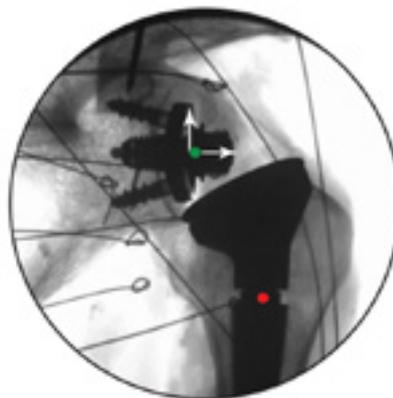
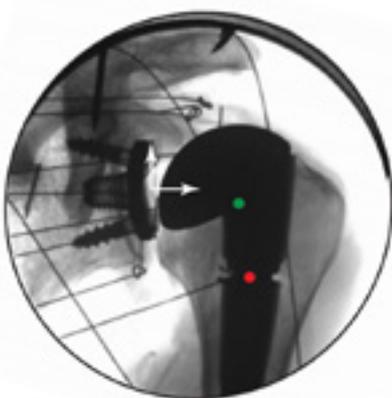
Distal biceps tendon injuries include acute complete and partial ruptures as well as chronic ruptures. In general, surgical treatment is recommended for most patients in order to restore normal muscle strength and function, particularly during forearm rotation-based activities. Different repair techniques 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 frontotemporal 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

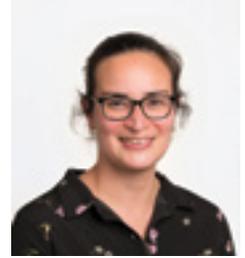
PROJECT CO-SUPERVISOR:

Georgina Craig

PROJECT AVAILABILITY:

- Master of Biomedical Science
- Honours

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

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 breakdown 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 an 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

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 tumorigenesis 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

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

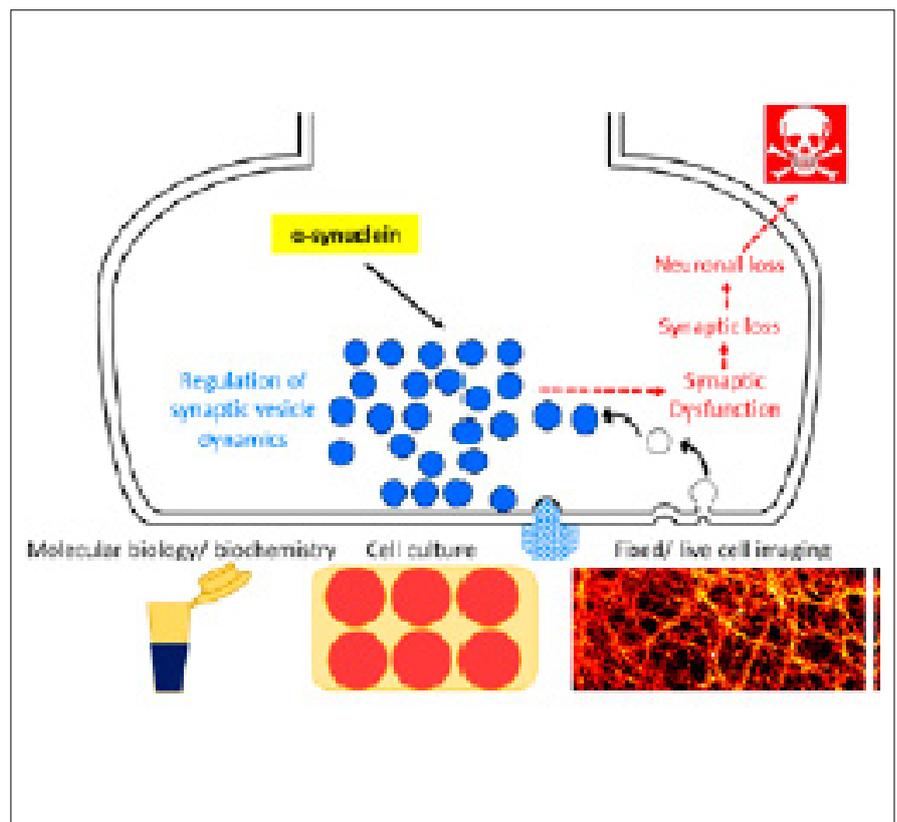
We have recently identified novel sites in alpha synuclein that are phosphorylated in an activity-dependent manner. This project will ascertain how phosphorylation at these distinct residues modulates the function of alpha synuclein as a regulator of presynaptic activity.

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: HOW DOES OXYTOCIN CHANGE SOCIAL BEHAVIOUR IN A MOUSE MODEL OF AUTISM SPECTRUM DISORDER?

Among all people with ASD, 70% report having a profound or severe core activity limitation, needing help or supervision to navigate communication, self-care and mobility. There are no treatments for ASD. While applied behavioural therapy has a moderate effect on reducing the symptoms of ASD, it is time consuming, costly and not easily accessed by all. The neuropeptide oxytocin has been explored as a treatment for ASD due to its role in social bonding, however to date, significant limitations in how these compounds cross the blood brain barrier have led to lack of efficacy. Our collaborators have designed novel oxytocin compounds and this project aims to test their efficacy in improving social behaviour in a genetic mouse model of Autism Spectrum disorder. This project will suit someone who is excited about handling mice and has a high attention to detail.

PROJECT SUPERVISOR:

Dr Emma Burrows

PROJECT CO-SUPERVISOR:

Prof Anthony Hannan

PROJECT AVAILABILITY:

- Honours

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 use 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 effects 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:

Prof. Anthony Hannan

PROJECT CO-SUPERVISOR:

Dr Carolina Gubert

- M.Phil/PhD

PROJECT AVAILABILITY:

- Honours
- Master of Biomedical Science

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

Email: yankadeva@unimelb.edu.au

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

LAWRENCE GROUP



Contact: Prof Andrew Lawrence

Email: Andrew.lawrence@florey.edu.au

Location: Florey Institute of Neuroscience and Mental Health

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

PROJECT: MUSCARINIC RECEPTORS IN ALCOHOL-SEEKING

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

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

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

PROJECT SUPERVISOR:

Dr Leigh Walker

PROJECT CO-SUPERVISOR:

Prof Andrew Lawrence

PROJECT AVAILABILITY:

- Master of Biomedical Science
- PhD

PROJECT: CONTEXT-INDUCED RELAPSE TO ALCOHOL-SEEKING AFTER VOLUNTARY ABSTINENCE

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

PROJECT SUPERVISOR:

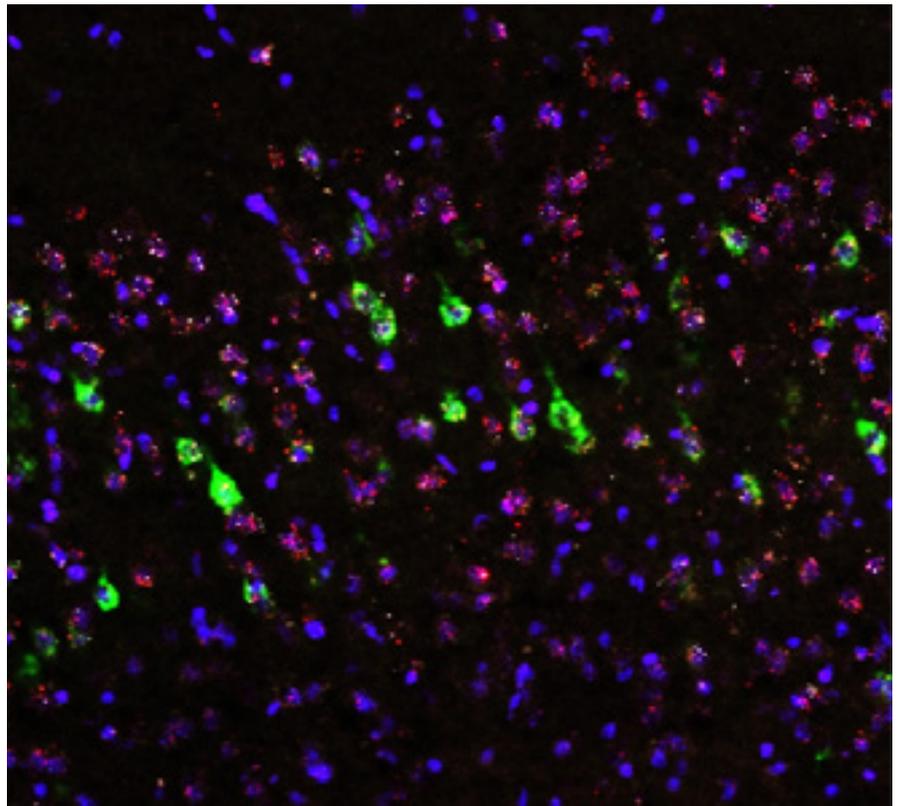
Dr Erin Campbell

PROJECT CO-SUPERVISOR:

Professor Andrew Lawrence

PROJECT AVAILABILITY:

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



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

PROJECT: THE OXYTOCIN SYSTEM IN SUGAR AND ALCOHOL INTAKE

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

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

PROJECT SUPERVISOR:

Dr Phil Ryan

PROJECT CO-SUPERVISOR:

Prof Andrew Lawrence

PROJECT AVAILABILITY:

- M.Phil/PhD
- Master of Biomedical Science

PROJECT: INVESTIGATING ALCOHOL-RELATED DEMENTIA

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

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

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

PROJECT SUPERVISOR:

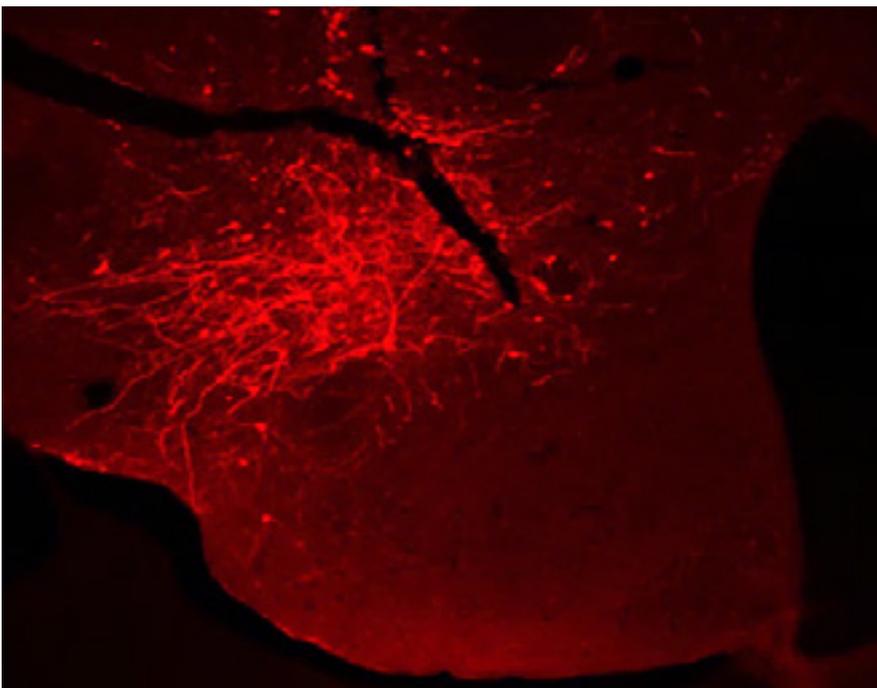
Dr Christina Perry

PROJECT CO-SUPERVISOR:

Prof Andrew Lawrence

PROJECT AVAILABILITY:

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



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

MACFIELD GROUP

Contact: Prof Vaughan Macefield
Email: Vaughan.macefield@baker.edu.au
Location: Baker Heart and Diabetes Institute



PROJECT: INVESTIGATING VESTIBULOSYMPATHETIC REFLEXES IN HUMANS

While several methods to activate the human vestibular apparatus have been used, galvanic vestibular stimulation (GVS) is a means of selectively modulating vestibular afferent activity via electrodes over the mastoid processes, causing robust vestibular illusions of side-to-side movement. Sinusoidal GVS (sGVS) causes partial entrainment of sympathetic outflow to muscle and skin. Modulation of muscle sympathetic nerve activity (MSNA) and skin sympathetic nerve activity (SSNA) from vestibular inputs competes with baroreceptor inputs, with stronger temporal coupling to the vestibular stimulus being observed at frequencies remote from the cardiac frequency. Moreover, the vestibular modulation of SSNA, but not MSNA, is augmented in individuals experiencing nausea. In this project we will extend our work on investigating vestibulosympathetic reflexes in humans, exploring how the frequency and pattern of stimulation modulates sympathetic outflow to muscle and skin. MSNA and SSNA can be recorded directly via metal microelectrodes inserted percutaneously into a peripheral nerve in awake humans (microneurography), and the student will acquire the skills for recording and analysing MSNA and SSNA, which can then be applied to a more detailed PhD project.

PROJECT SUPERVISOR:

Prof Vaughan Macefield

PROJECT CO-SUPERVISOR:

Dr Tye Dawood

PROJECT AVAILABILITY:

- Honours
- Master of Biomedical Science

PROJECT: THE CONTRIBUTION OF THE DORSOLATERAL PREFRONTAL CORTEX TO THE CONTROL OF BLOOD PRESSURE

The sympathetic branch of the autonomic nervous system plays a critical role in the control of blood pressure, both through its effects on the heart and, importantly, through the beat-to-beat control of blood flow through systemic blood vessels. Arterioles in the skeletal muscles are particularly important in this regard (the muscle vascular bed has a very high volume), and an increase in muscle sympathetic nerve activity (MSNA) is known to occur during psychological stress. MSNA can be recorded directly via metal microelectrodes inserted percutaneously into a peripheral nerve in awake humans (microneurography), and by recording MSNA at the same time as performing functional Magnetic Resonance Imaging (fMRI) of the brain we have shown that the dorsolateral prefrontal cortex (dlPFC) is involved in the regulation of MSNA. Here we shall use transcutaneous Direct Current Stimulation (tcDCS) and transcutaneous Alternating Current Stimulation (tcACS), delivered by surface electrodes applied to forehead, to change the activity of the dlPFC, and thereby investigate how such changes in activity modulate MSNA and blood pressure. The student will acquire the skills for recording and analysing MSNA, skills which can then be applied to a more detailed PhD project.

PROJECT SUPERVISOR:

Prof Vaughan Macefield

PROJECT CO-SUPERVISOR:

Dr Tye Dawood

PROJECT AVAILABILITY:

- Master of Biomedical Science

PROJECT: INVESTIGATING THE CONTRIBUTIONS OF THE VAGUS NERVE TO CARDIOVASCULAR CONTROL VIA INTRANEURAL RECORDINGS FROM THE CERVICAL VAGUS NERVE IN HUMANS

While we have learnt much about the role of the sympathetic nervous system in cardiovascular control from direct intraneural recordings of muscle sympathetic nerve activity (MSNA) in humans, our understanding of the contributions of the parasympathetic nervous system to control of the heart is indirect, based largely on assessment of heart rate variability (HRV). Now, for the first time, we have succeeded in making single-unit recordings from the human vagus nerve, by inserting a tungsten microelectrode through the skin of the neck and directing it into the nerve under ultrasound guidance. We have obtained preliminary data on the behaviour of cardiac parasympathetic axons but there is much to learn about the behaviour of the low-pressure baroreceptors in the atria and high-pressure baroreceptors in the aortic arch, for example. Aspects of this study will suit an Honours project, or more in-depth investigation would suit a Masters or PhD project.

PROJECT SUPERVISOR

Prof Vaughan Macefield

PROJECT CO-SUPERVISOR

Dr Tye Dawood

PROJECT AVAILABILITY

- Honours
- PhD
- Master of Biomedical Science

PROJECT: THE EFFECTS OF PAIN ON THE SYMPATHETIC AND IMMUNE SYSTEMS

Chronic pain - now defined as ongoing pain lasting more than 3 months - is frequently established from activation of nociceptors located in deep tissues such as muscle, but can be sustained in the absence of persistent peripheral noxious input by plastic changes within the brain. The incapacitating effects of long-lasting pain are not just psychological - reflexes driven by nociceptors during the establishment of chronic pain may cause serious physiological consequences that affect many systems, including the cardiovascular system. Using a model of experimental muscle pain - intramuscular infusion of hypertonic saline - we have shown that long-lasting muscle pain causes a sustained increase in muscle vasoconstrictor drive, blood pressure and heart rate in some subjects but sustained decreases in others. This may explain why some people develop high blood pressure following surgery, but why this occurs we do not know. The purpose of this project is to understand the processes by which noxious stimulation causes an increase in muscle vasoconstrictor drive and blood pressure in some people, but not in others. By recording muscle sympathetic nerve activity (MSNA) at the same time as performing functional magnetic resonance imaging (fMRI) of the brain we have recently identified differences in specific regions of the brain in a group showing an increase in MSNA and blood pressure and a group showing a decrease.

The current project will determine whether the differential sympathetic responses to muscle pain also lead to differences in inflammatory markers. The project will combine microelectrode recordings of MSNA in awake human subjects with intravenous blood sampling at rest and during one hour of experimental muscle pain. This approach will allow us to determine whether sympathetic activation leads to increases in release of inflammatory products, which in turn may contribute to long-term changes in the brain. The student will acquire the skills for recording and analysing MSNA, skills which can then be applied to a more detailed PhD project.

PROJECT SUPERVISOR:

Prof Vaughan Macefield

PROJECT CO-SUPERVISOR:

Dr Tye Dawood

PROJECT AVAILABILITY:

- Honours
- Master of Biomedical Science







Contact: Gawain McColl

Email: gmcoll@unimelb.edu.au

Location: Kenneth Myer Building

Website: www.florey.edu.au/science-research/scientist-directory/dr-gawain-mccoll

The McColl group 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 provide a wealth of information about the biochemical systems and fundamental biological processes. Despite the relative simplicity of these animals the conservation of genetic and disease pathways between these nematodes and higher eukaryotes make it an effective *in vivo* model for study ageing and disease mechanisms.

PROJECT: AGEING, IRON AND NEURODEGENERATION

Age is the single biggest risk factor for major neurodegenerative diseases, such as Alzheimer's and Parkinson's disease. How ageing drives disease susceptibility is a fundamental but poorly understood question. To solve the mystery of brain ageing we propose to first understand it in a simpler animal. Our laboratory takes a fresh approach, using the nematode *Caenorhabditis elegans*, with its well-developed genetics, to explore the biological roles of iron. Metal ions, including those of iron, are essential for life with approximately half of all proteins using a metal ion co-factor. However, excess metal ions can be highly toxic. Organs such as the brain accumulate 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

MCDUGALL 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: 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 vitro slice electrophysiology. Optogenetic 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 optogenetic 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:

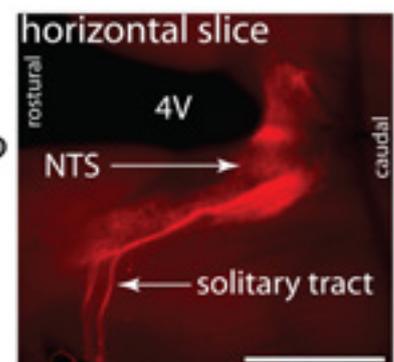
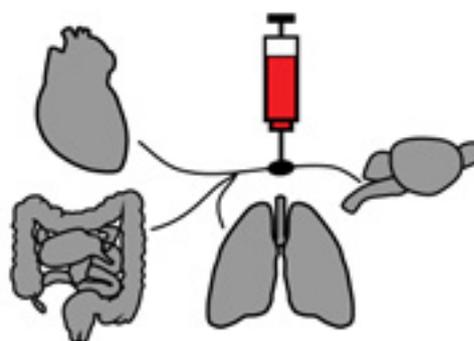
Dr Stuart McDougall

PROJECT CO-SUPERVISOR:

Professor Andrew Allen

PROJECT AVAILABILITY:

- Master of Biomedical Science
- Honours



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





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: MEASURING WHOLE BRAIN ACTIVITY DURING BEHAVIOUR

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

Here, memory formation and cortical activity during learning and decision making will be addressed using a widefield microscope which enables the surface of the entire mouse cortex to be measured. Here, using transgenic 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

PANG GROUP



Contact: Dr Terence Pang

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Location: Florey Institute of Neuroscience and Mental Health

Website: go.unimelb.edu.au/wx5j
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:

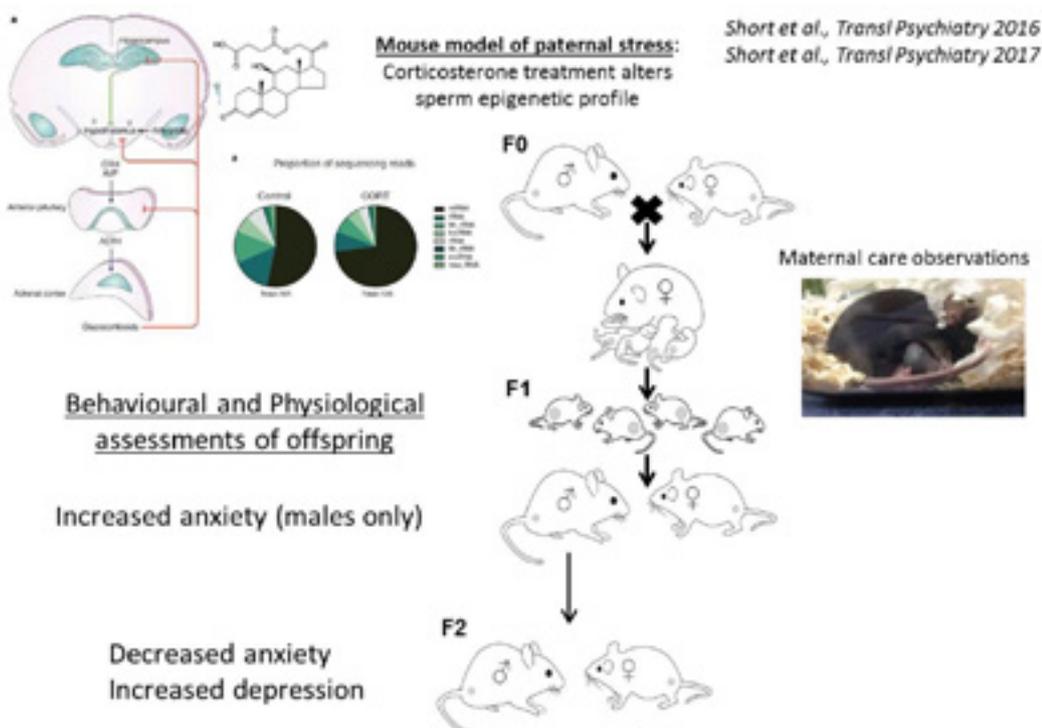
Dr Terence Pang

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:

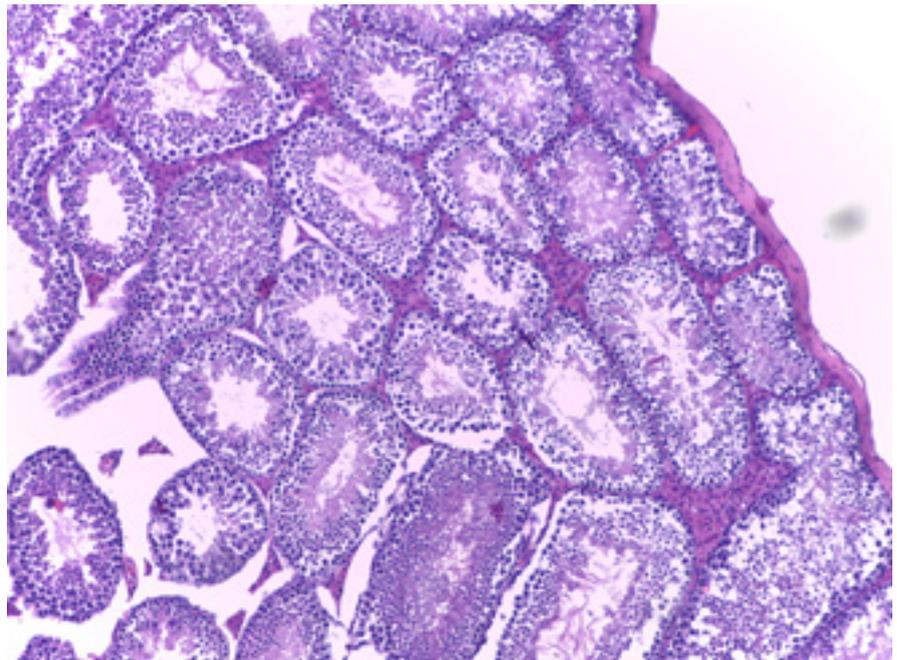
Dr Terence Pang

PROJECT CO-SUPERVISOR:

Prof David Gardner (School of Biosciences)

PROJECT AVAILABILITY:

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



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 stroke 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

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 stroke 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

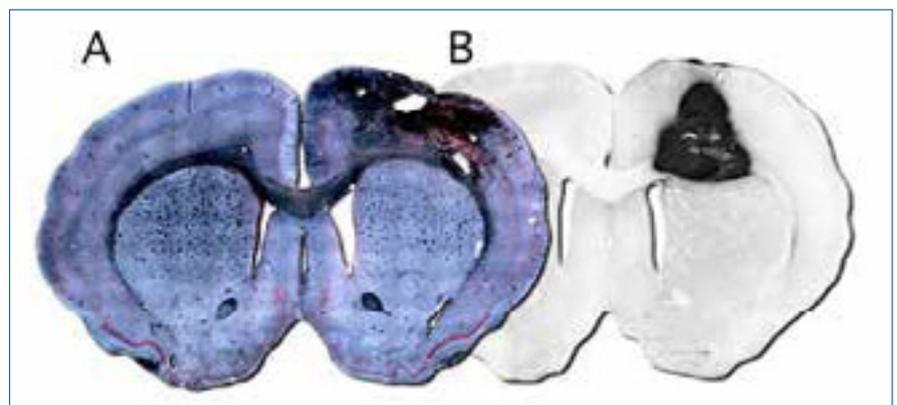


Figure. A) Damage to the cortex caused by focal ischemia. B) A stem cell derived graft of new cortical neurons to replace those lost to the ischemic damage.

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

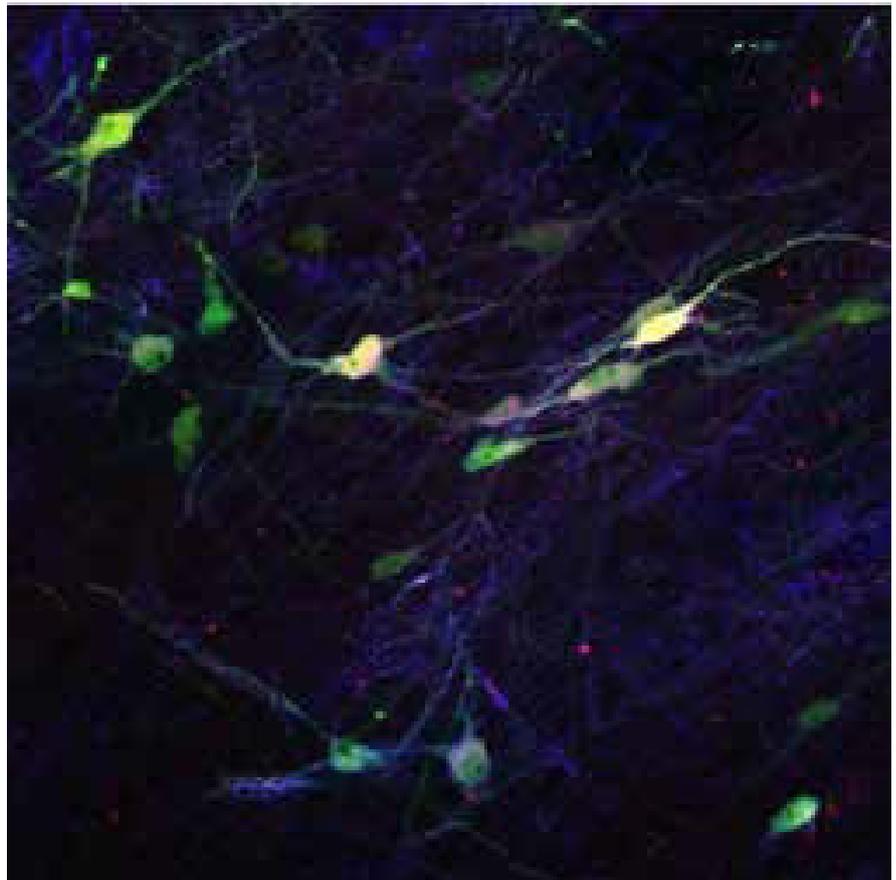


Figure: Functional midbrain dopamine neurons generated from human pluripotent stem cells

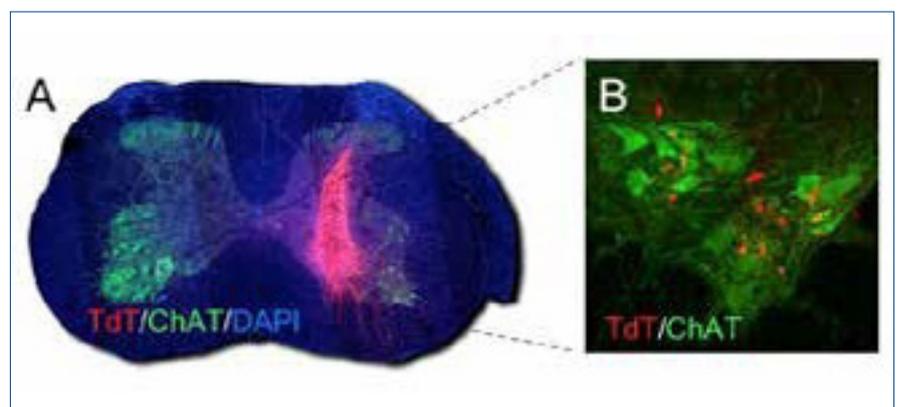


Figure. A) Graft of human stem cell derived neurons engineered to express a fluorescent protein (TdT) to allow for identification in the host brain. B) The transplanted neurons migrate to and intermingle with the diseased host motor neurons (ChAT) and may provide trophic support

Contact: A/Prof Bradley Turner

Email: bradley.turner@florey.edu.au

Location: Florey Institute of Neuroscience and Mental Health

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

PROJECT: INVESTIGATING THE AUTOPHAGY PATHWAY IN A NOVEL C9ORF72 MOUSE MODEL OF MOTOR NEURON DISEASE

Motor neuron disease (MND) is a neurodegenerative disease characterised by cytoplasmic accumulation and aggregation of proteins which are implicated in motor neuron death. Strategies that improve proteostasis and clear these misfolded proteins in motor neurons are therefore an attractive therapeutic approach for MND. Our group is interested in autophagy, the main catabolic pathway in neurons that targets and degrades misfolded proteins, aggregates and damaged organelles. C9ORF72 mutation is the largest genetic cause of MND affecting 40% of familial MND cases and 8-10 % of sporadic ALS. This project will investigate the autophagy pathway in a novel C9ORF72 mouse model and will employ advanced microscopy, immunohistological and image analysis techniques.

PROJECT SUPERVISOR:

A/Prof Bradley Turner

Project Co-supervisor:

Dr. Nirma Perera

PROJECT AVAILABILITY:

- Honours

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





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