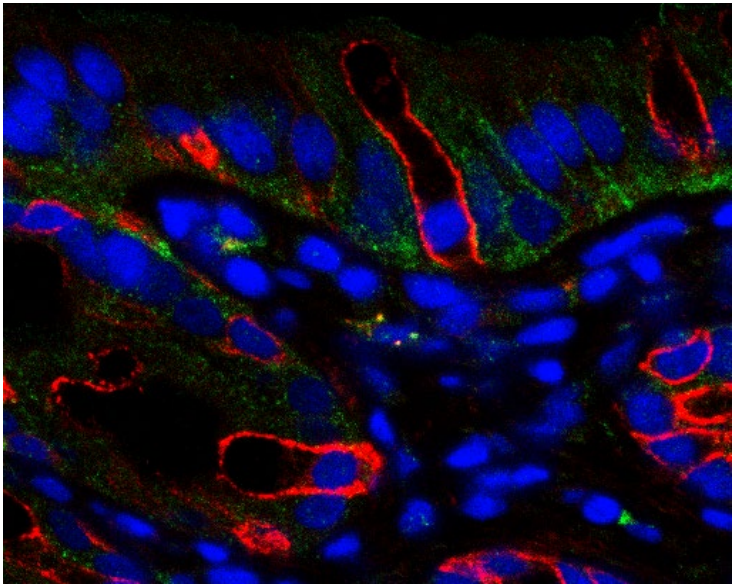


Physiology

400-Level Information 2023

400-level in the Department of Physiology 2023

If you are interested in a 400-level qualification in the Department of Physiology, as well as obtaining the necessary grades to be eligible (see "400-level Degree Options and Entry Requirements" below), you will need to secure a supervisor for your research project. The process for arranging a PHSL/NEUR PGDipSc or BSc (Hons) project, or a FUHB BBiomedSc (Hons) project in the Department of Physiology is below.

How to apply for a research project

1. Read the project descriptions (Appendix I).
2. E-mail the supervisors offering the projects in which you are interested to arrange a meeting to discuss the projects in-person or by Zoom.
3. Decide the projects for which you would like to be considered (up to three, in rank order) and the qualification for which you are applying.
4. Complete the online application form (link below) by the **11th November 2022**: https://forms.office.com/r/ueP1xCx6rg
   Late applications will only be considered if there are projects still available.

What happens next?

1. Your research project application and academic record will be given to the academics with whom you are interested in working, who will decide on whether to accept your application.
2. You will be informed of your application outcome by email in **early-December**.
3. If your research project application is successful:
   a. For **PGDipSci** or **BSc (Hons)**, complete your formal application for entry on eVision by **10th December**. Once we (or NEUR) confirm admission with the Division of Sciences Administration, you will be notified of acceptance on eVision.
   b. For **BBiomedSc (Hons)**, entry is subject to approval of the Pro-Vice-Chancellor (Health Sciences) on the advice of the Board of Studies for Biomedical Sciences. Acceptance into the programme is organised by the BBiomedSc Administration but is dependent on securing a research project.
4. If you are eligible but not matched with any of your choices, you will be provided an opportunity to discuss alternative projects with other supervisors who still have projects available.

400-level Scholarships and Stipends

Neither the University nor the Department offer scholarships or stipends for 400-level students. BBiomedSc, Māori and Pasifika students who gain high grades at 300-level can be awarded a small University of Otago Scholarship for 400-level. See www.otago.ac.nz/bms/postgraduate/index.html.

Questions? Contact:

- Prof Colin Brown (colin.brown@otago.ac.nz), 400-level convener, for questions about the 400-level course.
- the relevant supervisor for questions about the projects.
- physiology@otago.ac.nz for questions about your Research Project application.

400-level Degree Options and Entry Requirements

PGDipSci

Prerequisites: BSc including at least a B average (B+ recommended) in four of PHSL 341, 342, 343, 344, 345 or equivalents.

PGDipSci Course: two of PHSL 471, 472 and 473 (20 pts each), PHSL 474 (20 pts) and PHSL490 (60 pts).

BSc (Hons)

Prerequisites: Any four of PHSL 341, 342, 343, 344 and 345 plus an approved fifth paper at 300-level (or a fifth PHSL 300 paper) with at least a B+ average in the four PHSL 300 papers. Two further papers at 200-level or above are also recommended.

BSc (Hons) course: two of PHSL 471, 472, 473 (20 pts each) PHSL 474 (20 pts) and PHSL 490.

BBiomedSc (Hons) in Functional Human Biology

Prerequisites: A BBiomedSc degree with an average grade of at least B+ for the four prescribed 300 papers, must have passed a fifth 300-level paper in their third year of study (for a total of 90 points at 300-level), and should normally have passed papers worth at least 126 points at 200-level or above in their third year of study.

BBiomedSc (Hons) course: A 120-point programme, comprising a research thesis and course work.

See: https://www.otago.ac.nz/courses/qualifications/bbiomedschons.html.

N.B. Entry into the two-year MSc programme is organized through a different process; please contact the Physiology Postgraduate Coordinator, Assoc Prof Jeff Erickson (jeff.erickson@otago.ac.nz) for information on the process.

400-level Papers

PHSL 471 Systematic Physiology, PHSL 472 Neurophysiology and PHSL 473 Cellular Physiology

These 20-point papers each consist of seminars on research frontiers in physiology. Each paper requires preparation and participation (e.g. discussion, presentation, etc.), and is assessed by written examination.

PHSL 474: Research Topics

This 20-point paper is a self-directed literature survey of physiology topics that complement, but are distinct from, the research project. It is specifically designed for each student, guided by the supervisor and is internally assessed by three essays.

PHSL 490: Research Dissertation (Hons)

This is a 60-point laboratory project involving original research and is assessed by a dissertation in the form of a thesis. All steps of the project are guided by the supervisor. PHSL 490 also includes oral presentations to the Department in April and September/October. Thesis submission is in late October. A 40-point PHSL 480 Research Project is also available for PGDipSci students, but we do not recommend this paper.

Appendix I: Research Projects

Our research falls into the following main areas:

- **Cardiovascular Physiology:** Jeff Erickson, Pete Jones, Rajesh Katare, Regis Lamberts, Michelle Munro, and Daryl Schwenke.
- **Neurophysiology:** Colin Brown, Rosie Brown, Rebecca Campbell, Tanya Cully, Karl Iremonger, Pete Jones, Phil Sheard, and Alex Tups.
- **Membrane & Ion Transport:** Andrew Bahn, Martin Fronius (not available in 2023), Kirk Hamilton, and Fiona McDonald.

Cardiovascular Physiology Projects

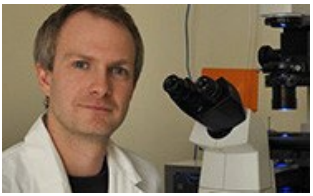
Associate Professor Jeff Erickson & Dr Luke Worthington (jeff.erickson@otago.ac.nz)

The role of CaMKII in diabetes-induced heart failure

CaMKII activation is a primary pathological event in heart failure and arrhythmia, particularly for patients with diabetes mellitus. Thus, CaMKII has emerged as a potential therapeutic target in the treatment of heart disease. With this in mind, our research focuses on investigating the role of CaMKII in the diabetic heart. Contributions by a motivated 400 level student would be possible for a project examining cardiac function in diabetic animal models using protein blotting, histochemistry, and cell imaging techniques.

Associate Professor Pete Jones (pete.jones@otago.ac.nz)

Role of RyR2 mediated calcium release in arrhythmia and Alzheimer's disease



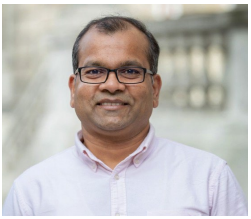
We are seeking students to join our research group for various projects that relate to the following research theme: Calcium release is critical for contraction in the heart and synaptic transmission in the brain. In both tissue types, the ryanodine receptor (RyR2) mediates a large part of this release. When the carefully controlled release of calcium through RyR2 goes wrong it leads to disease. Our lab aims to understand the molecular mechanisms which lead to abnormal RyR2 function.

Several projects are available looking at the function and structure/ location of RyR2 within cardiac cells and neurons with the purpose of better understanding arrhythmias and Alzheimer's disease.

New methodology for high speed, live cell, super-resolution imaging

We are seeking students interested in biophysics, particularly optic imaging modalities. Calcium signalling is a common secondary signalling pathway in many cell types. Typically, these calcium signals occur very quickly and in carefully controlled areas 'micro domains' of the cell. The very fast, very localised nature of these events make them impossible to observe using conventional microscopy.
This project, a collaboration with Dr Amita Deb in the Department of Physics, aims to develop a new method of super-resolution microscopy that will permit the rapid imaging of calcium signalling in microdomains of live cells. The microscope will be validated by monitoring changes in ryanodine receptor (RyR2) mediated calcium release in cardiac cells and neurons.

Associate Professor Rajesh Katare (rajesh.katare@otago.ac.nz)



Understanding molecular mechanisms and development of novel therapies for diabetic heart disease

Our team is interested in development of mechanism-based novel therapies for the treatment of diabetic heart disease. We are seeking students to join our research group for various projects that relate to the following research themes.

MicroRNAs as molecular mediators and therapeutic target for diabetic heart disease

Our recent studies have identified a strong association between the microRNAs and cardiovascular disease. We are now aiming to understand the mechanisms how microRNAs induced heart disease in diabetic individuals and test whether microRNAs could be a possible therapeutic target.

Stem cells for the regeneration of diseased heart

Autologous stem cell transplantation is considered as the next generation of drug treatment in patients with cardiovascular disease. However, the best source of stem cells for the regeneration of heart is still not known. We aim to identify the best stem cells for regeneration of diseased heart with the aid of clinical samples from Dunedin Hospital.

Associate Professor Regis Lamberts & Dr Hamish Aitken-Buck

(regis.lamberts@otago.ac.nz/hamish.aitken-buck@otago.ac.nz)

Understanding heart fat and cardiovascular disease

Excessive deposition of heart fat, termed epicardial adipose tissue (EAT), has been strongly associated with measures of cardiovascular disease risk. How the heart fat exactly interacts with the myocardium, whether inflammation is involved, and if potential sex differences occur, is however unknown. Our group has begun addressing this poor understanding in EAT samples procured from cardiac surgery patients and post-mortem cases. We are seeking a motivated 400-level student to join our productive research group and continue uncovering the characteristics of EAT and its interaction with the myocardium. This project provides the opportunity to learn several molecular techniques (PCR, protein quantification, immunohistochemistry, ELISA), as well as how to apply contemporary statistical analyses to larger clinical datasets.

Dr Michelle Munro (michelle.munro@otago.ac.nz)

Calcium handling proteins in heart disease

The normal contraction of the heart relies on the tightly regulated movement of calcium within the myocytes. Calcium mishandling occurs in a number of cardiac diseases, which can lead to impaired contractility and the development of irregular contractions (arrhythmias). The release of calcium from the sarcoplasmic reticulum (SR) via the ryanodine receptor (RyR2) is critical for cardiac function. However, abnormal RyR2 activity has been linked to the development of cardiac disease, including arrhythmia and heart failure. Calsequestrin (CSQ2) is a protein within the SR that buffers calcium and regulates RyR2 function – a mechanism which may be altered in cardiac pathologies. Projects are available to study the organisation, expression and regulation of CSQ2 and RyR2 in cardiac diseases including atrial fibrillation, diabetes and heart failure. A range of techniques are used in our lab including calcium imaging, immunohistochemistry, fluorescent imaging, super-resolution microscopy and western blotting.

Atrial fibrosis and t-tubules in human cardiac disease

The transverse (t-)tubules are key structures in cardiomyocytes which enable the rapid and synchronised contraction of the heart. Their organisation and importance in cardiac function has been well established in the ventricle. Extensive loss and remodelling of the t-tubule network is known to occur in settings of heart disease. Fibrosis is one mechanism known to contribute to this remodelling in the ventricle. However, little is known about the role of t-tubules in the atria and in atrial cardiomyopathies. We have recently confirmed the presence of t-tubules in human atrial myocytes. This project will use a combination of immunofluorescence and confocal microscopy to investigate if these t-tubules undergo remodelling in atrial tissue from patients with cardiac disease, and determine the potential role of fibrosis in remodelling.

Associate Professor Daryl Schwenke (daryl.schweneke@otago.ac.nz)

Background & Project Objectives:

My research team is interested in how the brain communicates with the heart for the precise control of cardiac function, and how this highly coordinated communication is dangerously disrupted following an acute myocardial infarction and in diabetic heart disease. In addition, I am also interested in the potential mechanism(s) that underpin the onset of pulmonary hypertension, with a recent interest in the potential role of epithelial sodium channel in driving disruption of pulmonary function.

A variety of research projects are available for a highly motivated BSc(Hons) candidate, including:

- identifying neuronal pathways in the brain-heart axis that are damaged in diabetes, which underpins the onset of Cardiac Autonomic Neuropathy in diabetes (co-supervised with Assoc. Prof Rajesh Katare).
- assessing the benefits of exercise training for ‘re-wiring’ the brain-heart neural axis to reduce heart damage following a myocardial infarction (co-supervised with Prof Colin Brown)
- revealing the role of the epithelial sodium channel (ENaC) in driving the onset of pulmonary function hypertension (co-supervised with Dr Martin Fronius).
- assessing the impact of myocardial infarct size on sympathetic neuronal activation and, thus, mortality in acute heart failure (co-supervised with Prof Colin Brown).

Neurophysiology Projects

Professor Colin Brown (colin.brown@otago.ac.nz)

Hypothalamic regulation of reproductive and cardiovascular function

Our research group principally uses electrophysiology and immunohistochemistry in preclinical animal models to determine how the brain controls birth, lactation, and cardiovascular function. Our main focus is on how oxytocin and vasopressin contribute to preterm labour, high blood pressure and heart problems. Various projects are available around these topics.

Dr Rosie Brown (rosemary.brown@otago.ac.nz)

Rescuing maternal care-giving behaviour in a mouse model of maternal obesity

During pregnancy, hormones act on neural circuitry to bring about the timely display of maternal care-giving behaviour by the mother. Maternal obesity is associated with numerous pregnancy complications including increased risk for postpartum mood disorders. We and others have shown that mice on a high fat diet display severely impaired maternal care of offspring. Maternal obesity is also associated with decreased hormone production from the placenta, including the prolactin family of hormones that are critical for maternal care. The aim of this project is to test whether prolactin supplementation can rescue maternal care in a mouse model of maternal obesity.

Interrogating a neural circuit regulating maternal care-giving behaviour

Neurons expressing the prolactin receptor in the brain are essential for maternal care-giving behaviour and survival of new-born offspring. This project will test how specific neural circuits govern discrete aspects of maternal care-giving behaviour, and whether stimulation of circuits can drive these behaviours in animals that would normally ignore new-born young.

Professor Rebecca Campbell (rebecca.campbell@otago.ac.nz)

Using pre-clinical models to understand the PCOS brain

Research in our lab is aimed at understanding the brain circuits that regulate fertility and the central defects that contribute to infertility. We are particularly focused on understanding how brain wiring and communication is altered in the common endocrine disorder Polycystic Ovary Syndrome (PCOS). For the appropriate student, a 400-level project will be developed to better understand the central defects that may underpin the neuroendocrine pathology of PCOS in a pre-clinical model of the syndrome. The project will likely involve working with transgenic mouse models, immunohistochemistry, light and confocal microscopy, and the application of imaging software and analysis.

Dr Tanya Cully (tanya.cully@otago.ac.nz)

Calcium and ROS signalling in skeletal muscle function

Our research lab has Honours projects focusing on the interplay between calcium and reactive oxygen signalling in healthy and diseased skeletal muscle. Calcium is known to have a critical role in the degenerative phase of many muscular diseases that leads to muscle degeneration and frequent attempts at regeneration. A leaky calcium channel in skeletal muscle can be a result of the influence of reactive oxygen species (ROS) which can promote damage and inflammation in the muscle. Projects will focus on rodent models and may utilise several techniques, such as biochemical measurements, DNA electroporation and microscopy. We will seek to understand the role of two ROS producing isoforms and their influence on calcium handling in different skeletal muscle fibre types, to gain a greater understanding of these processes as well as identify potential drug targets.

Dr Karl Iremonger (karl.iremonger@otago.ac.nz)

Regulation of neural circuits controlling stress

Our laboratory focuses on understanding hypothalamic neural circuits which control stress. Corticotropin-releasing hormone (CRH) neurons are activated in response to stress and are responsible for controlling the levels of stress hormones in the body. Research projects in the lab focus on determining how the excitability of CRH neurons is controlled before, during and after stress.

Associate Professor Phil Sheard (phil.sheard@otago.ac.nz)

Nerve and muscle ageing

We investigate the cellular processes that underpin age-related deterioration of nerve and muscle function. Projects are developed in collaboration with the student, but typically involve use of immunohistochemistry and microscopy techniques to examine how important cell structures involved in nerve and muscle function change as the organism ages.

Associate Professor Alex Tups (alexander.tups@otago.ac.nz)

Neuroendocrine control of obesity and diabetes

If you want to find out why jetlag causes obesity or why Alzheimer's disease is called type 3 diabetes join the Tups lab for pursuing your BSc Honours studies. Projects are available to study the neuroendocrine control of obesity and glucose homeostasis or their interaction with the circadian clock as well and brain function. You can choose to either work with zebrafish or mouse models which we use to combine genetic, pharmacological, or nutritional manipulations with the assessment of metabolic health.

Membrane & Ion Transport Projects

Dr Andrew Bahn (andrew.bahn@otago.ac.nz)

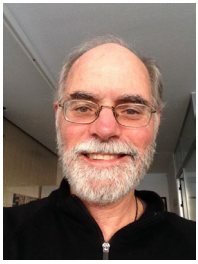
Disturbance of the 'Cellular uric acid homeostasis' as the driver for diabetes mellitus, hypertension, neurodegeneration and cancer

Our group is interested in how uric acid controls major intracellular metabolic signalling pathways (mTOR, AMPK, circadian rhythm) via ubiquitination in order to understand the onset of diabetes mellitus, hypertension, neurodegeneration and cancer. Uric acid transporters and especially GLUT9, ABCG2 or MRP4 are emerging as major players for 'cellular uric acid homeostasis' in many tissues controlling cellular redox and energy homeostasis as well as inflammation, ultimately defining cell fate and survival.

There are several projects available. Students who are interested in the topic and keen to meet a challenge to perform state of the art research are encouraged to apply.

Associate Professor Kirk Hamilton and Professor Fiona McDonald

(kirk.hamilton@otago.ac.nz/ fiona.mcdonald@otago.ac.nz)



The role of protein complexes in trafficking of ion channels in polarised epithelia

We have research interests is the molecular physiology, regulation and function of membrane ion channels of epithelial tissues. A/Prof Hamilton and Prof McDonald examine the molecular trafficking of epithelial ion channels including K^+ channels such as the Ca^{2+}-dependent K^+ channels KCa3.1 and KCa2.3, and the epithelial Na^+ channel, ENaC, respectively. We try to understand the protein complexes (Exocyst, Retromer, Retriever protein complexes) involved in the trafficking of KCa3.1, KCa2.3 and ENaC to the appropriate membranes of epithelial cells. We use a range of protein biochemistry, molecular biology, electrophysiological and imaging techniques. The implication of these results is to define novel trafficking partners of K^+ and Na^+ channels that may be used therapeutically in diseases.

Professor Fiona McDonald and Dr Michelle Munro

(fiona.mcdonald@otago.ac.nz/ michelle.munro@otago.ac.nz/)

The epithelial sodium channel and its effect on calcium signalling in breast cancer

Breast cancer is the most common cancer affecting New Zealand women and, 90% of breast cancer deaths occur due to metastasis whereby cells change their structure and shape, and begin to proliferate and migrate, contributing to breast cancer progression and metastasis. Our bioinformatic data suggests that high epithelial sodium channel (ENaC) expression is associated with better outcomes in breast cancer. Using cultured breast cancer cells, we have shown that increased ENaC expression reduces breast cancer migration and proliferation. Changes in cellular levels of both Na^+ and Ca^{2+} have been implicated in cancer cell migration and proliferation. We investigated if changes in ENaC levels alter Ca^{2+} handling in a model cell culture system. Our preliminary results suggest increased ENaC levels reduce Ca^{2+} leak. Therefore, this project will further investigate the interplay between Na^+ and Ca^{2+} using Ca^{2+} imaging, and appropriate blockers, to discover the mechanism that ENaC may be influencing to alter Ca^{2+} handling to reduce cell migration and proliferation in breast cancer cells.

Professor Fiona McDonald

(fiona.mcdonald@otago.ac.nz)

Epithelial sodium channel regulation of breast cancer progression

Breast cancer is the most common cancer affecting New Zealand women and, 90% of breast cancer deaths occur due to metastasis. A process called epithelial-mesenchymal transition (EMT), whereby cells change their structure and shape, and begin to proliferate and migrate, is thought to contribute to breast cancer progression and metastasis. However, these pathways are not well understood. Our novel data suggest that high levels of epithelial sodium channel (ENaC) expression in patient tumours correlates with a better prognosis, and that changes in ENaC expression level significantly alters breast cancer cell proliferation and migration.

We aim to determine the pathways associated with these changes and potential mechanisms for the role of ENaC in breast cancer. In this project you will use characterised breast cancer cell lines to investigate the effect of ENaC levels on one or more cancer hallmark including: cell migration, cell proliferation, invasion, epithelial integrity (cell-cell and cell-basement membrane interactions), cellular signalling pathways.