Te Tari Mātai Whaiaroaro

Department of Physiology

Taumata-400 2024

400-level 2024

Ngā whakamārama | Information

Te tukanga tono | Application process

Please read this document carefully because it contains important information about the 400-level programme in Physiology, including entry requirement and how to arrange a PHSL/NEUR PGDipSc or BSc (Hons), or BBiomedSc (Hons) project with a supervisor in the Department of Physiology.

Te tukanga tono | Application process

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 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 by the **10th November 2023**:
5. Late applications will be considered if there are projects available.

What happens next?

1. Your research project application and academic record will be given to the academic 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:
4. For **PGDipSci** or **BSc (Hons)**, complete your formal application for entry on eVision by **10th December 2023**. Once we (or NEUR) confirm admission with the Division of Sciences Administration, you will be notified of acceptance on eVision.
5. 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.
6. 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.

Ngā karahipi | Scholarships

The University offers various scholarships for 400-level students. In addition, Māori and Pacific Peoples students can apply for a School of Biomedical Sciences Scholarship for 400-level ($7,500 tuition fee waiver). The Department of Physiology also offers one stipend of $5,000 to a Māori or Pacific Peoples student undertaking a 400-level project in the Department, preferably in a neurophysiology topic.

Application instructions:

All scholarships can be found here.

Māori Biomedical Sciences Scholarships can be found here.

Pacific Peoples Biomedical Sciences Scholarships can be found here.

For the Māori or Pacific Peoples Physiology stipend, please forward a copy of a School of Biomedical Sciences application directly to phsl.400@otago.ac.nz.

Questions? Contact:

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

Ngā Herenga Tohu Paetahi | Degree Requirements

PGDipSci

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

Programme: PHSL 471 and 472 (20 pts each), PHSL474 (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.

Programme: PHSL 471 and 472 (20 pts each), PHSL474 (20 pts) and PHSL490 (60 pts).

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.

Programme: 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 Karl Iremonger (karl.iremonger@otago.ac.nz) for information on the process.

Pārongo Hōtaka | Programme information

PHSL 471 Systematic Physiology and PHSL 472 Neurophysiology

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

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.

Appendix I: Research Projects

Our research falls into the following main areas:

- **Cardiovascular Physiology:** Tanya Cully, Jeff Erickson, Martin Fronius, Pete Jones, Rajesh Katare, Regis Lamberts (not available in 2024), Megan Leask, Michelle Munro, and Daryl Schwenke (not available in 2024).
- **Neurophysiology:** Colin Brown, Rosie Brown, Rebecca Campbell, Karl Iremonger (not available in 2024), Joon Kim, Phil Sheard, and Alex Tups.
- **Membrane & Ion Transport:** Andrew Bahn, and Fiona McDonald.

Cardiovascular Physiology Projects

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

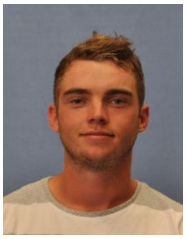
Investigating cardiac pathophysiology in a mouse model of skeletal muscle and cardiac disease

The work in this project would contribute to a larger collaboration between the Erickson and Cully labs. This project involves echocardiogram and ECG measurements in a preclinical mouse model of Duchenne Muscular Dystrophy (DMD). Currently, there is no cure for DMD with the leading cause of patient mortality being cardiorespiratory failure.

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

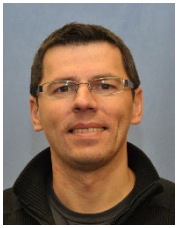
The role of CaMKII in diabetes-induced heart failure

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 Martin Fronius (martin.fronius@otago.ac.nz)

Investigating the effect of vapes on lung epithelia



The project aims to investigate if and how vapes interfere with ion transport in human lung epithelial cells. Gas exchange and the innate immune system in our lungs rely on transepithelial ion transport processes, facilitated by the epithelia covering the surfaces of the lungs. Cigarette smoke has been identified to interfere with ion transport processes, which contributes to lung pathologies including chronic bronchitis and chronic obstructive pulmonary disease (COPD). Although the number of cigarette smokers decreased over time, vaping is becoming more and more popular. Vaping is perceived as a 'healthy' alternative to smoking. However, there are growing reports of lung damage associated with vaping termed e-cigarette or vaping product use–associated lung injury (EVALI). Interestingly, the damage observed is different in comparison to cigarette smoke.

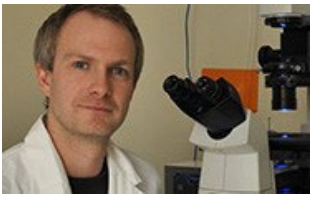
The project will expose human lung epithelial cells (H441 cells) to vapes and measure how this affects ion transport processes by performing Ussing chamber electrophysiology. The study will identify a putative mechanism by which vaping interferes with normal epithelial cell function that is crucial for normal breathing.

Characterising TRPV channel function underpinning hypothalamic vasopressin release

Vasopressin release from osmosensitive neurones in the hypothalamus is essential for maintaining plasma osmolality homeostasis and blood pressure regulation. Elevated vasopressin release is associated with hypertension indicating impaired function of these osmosensitive neurones. Osmosensitivity in these neurones relies on the function of Transient Receptor Potential Vanilloid (TRPV) ion channels. Activation of these channels in response to increased plasma osmolality activates the channels to depolarise the cell membrane potential. This increases action potential frequency and drives the exocytosis of vasopressin. The Fronius and C. Brown laboratories are interested in understanding the processes of how TRPV channels sense cell shrink and cell swell due to changes of plasma osmolality. Further, if changed TRPV channel function is a contributor to elevated vasopressin release in hypertension. The project provides the opportunity to study TRPV channel function by patch clamp electrophysiology and characterise how cell swell and shrink (mimicked by the application of positive and negative pressure) affects channel activity. Main goal of the study is to understand if and how TRPV channels contribute to hypertension.

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.

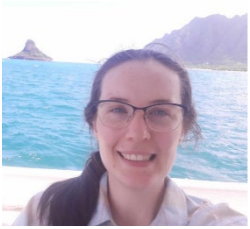
Associate Professor Rajesh Katare (rajesh.katare@otago.ac.nz)

Molecular mechanisms underlying healthy ageing

Ageing is an inevitable process accompanied by a gradual decline in physiological functioning. Advances in healthcare and improvements in diet have significantly increased life expectancy. However, this increased longevity has also led to a higher incidence of chronic diseases. The Honours project will explore the molecular mechanisms associated with cardiovascular disease. The project provides an opportunity to learn several molecular techniques, such as PCR, protein quantification, immunohistochemistry, and ELISA, and how to apply contemporary statistical analyses to larger clinical datasets.

Dr Megan Leask (Kāi Tahu) (megan.leask@otago.ac.nz) & Dr Hannah Darroch

The role of JAZF1 in diabetes in Māori and Pacific people



A genetic variant in Māori and Pacific peoples that lies in an enhancer region of a gene called JAZF1 has been identified that is strongly associated with type 2 diabetes. JAZF1 is expressed in many organs/tissues and is largely involved in regulating a cell's energy balance, sensitivity to insulin, and capacity to manage metabolic stress. Contributions by a motivated 400 level student would be possible for a project examining the effects of a zebrafish JAZF1 knockout on the brain, immune system and glucose homeostasis.

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. Projects are available to study the organisation, expression and regulation of key calcium handling proteins 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.

Neurophysiology Projects

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

Calcitonin receptor-like receptor regulation of vasopressin neuron activity

A calcitonin receptor-like receptor (CALCRL) variant is present in one third of individuals of Māori and Pacific descent but is virtually absent in individuals from outside Oceania. The variant is associated with low blood pressure in non-diabetic individuals but with high blood pressure in diabetic individuals. Hence, there might be a genetic contribution to blood pressure regulation by CALCR, which raises the possibility that a precision medicine approach could improve health outcomes in diabetes, particularly for Māori and Pacific individuals.

CALCRL is activated by adrenomedullin, which modulates blood pressure via inhibition of vasopressin (anti-diuretic hormone) release. Vasopressin stimulates the kidneys to reabsorb water and thereby reduce water loss in the urine. Genetically modified rats that express the CALCRL variant urinate excessively and have low blood pressure, suggesting that inhibition of vasopressin secretion might mediate the CALCRL variant effects on blood pressure. Vasopressin is secreted from the posterior pituitary gland by neuroendocrine hypothalamic neurons. This project will use multielectrode electrophysiology (Neuropixels) to determine whether vasopressin neurons of CALCRL variant rats have a reduced basal action potential firing rate and a reduced response to increased plasma osmolality (the primary physiological stimulus for vasopressin secretion) than vasopressin neurons of non-variant rats.

This research is supported by the Maurice Wilkins Centre (MWC) and subject to oversight by MWC Māori advisors.

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 Joon Kim (joon.kim@otago.ac.nz)

Our research group is interested in studying how the brain connects internal states with behaviour. Specifically, we aim to understand how stress states affect defensive behaviours, motivation, and mental health, by investigating the activity of hypothalamic CRH neurons. In our laboratory, projects start at the behavioural level using animal models. We will also manipulate the activity of CRH neurons to gain insights into their role in controlling the behaviour of interest.

For 2024, we are offering up to three projects that aim to link CRH neuron activity with specific changes in behaviours:

- **Stress and reward seeking behaviours**
- **Protective role of social connectedness on mental health during stress**
- **Singleness of action: defensive behaviours and competing motivations**

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

Age-related changes in neuromuscular systems

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. We will focus on mechanistic work to combine genetic, pharmacological, or nutritional approaches to find novel treatments for 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 and cancer

Our group is interested in how uric acid controls cellular plasticity by changing major intracellular signalling pathways such as mTOR, AMPK, TGFβ, FOXO1, or the inflammasome in order to understand the onset of diabetes mellitus 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 metabolism, redox homeostasis as well as inflammation, ultimately defining cell fate and survival. We are using cell and mouse models and by applying biochemical, molecular, and imaging techniques we are aiming to decipher the molecular mechanisms of cellular plasticity. There are several projects available. Students who are interested in the topic and keen to meet a challenge are encouraged to apply.

Professor Fiona McDonald (fiona.mcdonald@otago.ac.nz)

Trafficking of ion channels in polarised epithelia

Trafficking of epithelial ion channels to the correct membrane domain is required for optimal ion and water flow across epithelia. Correct trafficking of the Ca2+-dependent K+ channels KCa3.1 and KCa2.3, and the epithelial Na+ channel, ENaC is required to prevent conditions such as hypertension (ENaC). Trafficking of ion channels requires interaction with several protein complexes such as the Retromer and Retriever recycling complexes, or the exocyst complex for targeting to the basolateral membrane. In this project you will use a range of techniques such as protein biochemistry, molecular biology, electrophysiology and imaging to discover how ion channels traffic to their correct membrane domain. The implication of these results is to define novel trafficking partners of K+ and Na+ channels that may be used therapeutically in diseases.

Epithelial sodium channel and its effects on 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, contributes to breast cancer progression and metastasis. During EMT cancer cells lose their epithelial phenotype, including cell-cell and cell-

basement membrane connections, and gain mesenchymal characteristics, such as increased proliferation and migration. Our data has highlighted a role for the epithelial sodium channel (ENaC) in EMT, with a loss in ENaC expression potentially driving EMT. Projects will investigate the effect of ENaC on cancer hallmarks, signalling pathways, or Ca2+ levels in breast cancer cells, using techniques such as cell migration, cell proliferation, invasion, cell-extracellular matrix interactions, western blot and Ca2+ imaging.