School of Anatomy, Physiology and Human Biology

Student Research Projects for Honours, Masters and PhD Studies

2016
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Supervisor and Topic

**Supervision**

The role of the supervisor is to advise, guide and provide constructive feedback to the student through the processes of choosing a realistic topic, designing a project, doing the research and interpreting the findings and writing the dissertation.

Things to do before deciding on a supervisor:

- Talk with a few prospective supervisors about their research interests and prospective topics, as well as their styles of supervision and what they expect of their students; and
- Talk with your prospective supervisors’ current and former Honours and postgraduate students about their experiences.
- Things to discuss and negotiate with your supervisor very early in the program:
  - The regularity, timing and format of your meetings;
  - The type and level of assistance that you would like, and your supervisor is prepared to give, with respect to choosing a topic and setting goals; finding appropriate literature; collecting the data and information; analysing and interpreting your findings; planning the dissertation; and writing and reviewing the dissertation.

**Choosing a Topic**

Before deciding on a topic, it is usually a good idea to first identify one or more prospective supervisors according to the criteria above. Then, in consultation with your prospective supervisor/s, identify some possible topics and projects according to the following criteria:

- Choose an area that is sufficiently interesting to you to maintain your enthusiasm for a year-long project;
- Choose a topic in which you can identify questions to be answered or gaps to be filled in the current knowledge; and
- Find a project that is realistic for you to complete within the time allocated for your research and dissertation.

The tips above have been excerpted from the document “Preparing for Honours – Hints and Tips” from the following UWA Student Services website:
Information for Honours Applicants

In an Honours year, the learning emphasis is on completing an original research project. Projects are guided by academic staff who are internationally recognised in their specific fields of research. Students acquire the specialized skills required to complete their particular research project, and also develop generic research skills such as analytical and problem-solving abilities, and a variety of communication skills. These are not only vital for future success in research but stand graduates in good stead whatever career they may subsequently pursue. Throughout the year, students also work in close collaboration with a like-minded peer group and professional university staff.

Honours are available in the following discipline:

- Anatomy and Human Biology
- Physiology
- Neuroscience (by arrangement)
- Biomedical Science (by arrangement)

General information about Honours in Anatomy, Physiology and Human Biology can be found at http://www.aphb.uwa.edu.au/courses/honours.

Students can apply for a prestigious Dr Margaret Loman-Hall Honours Scholarships to support their studies. Further information is available at http://www.aphb.uwa.edu.au/students/scholarships.

Entry to Honours requires at least a 65% average in 24 points of level 3 units that are relevant to the honours discipline you wish to study. Enrolment must be full time but students may enter the course in February or July.

As a starting point, applicants should talk to potential supervisors. Research areas and associated staff can be found at http://www.aphb.uwa.edu.au/research.

Each year some suggested projects are posted on our honours website at http://www.aphb.uwa.edu.au/research/student-projects. If students wish to nominate and pursue topics of their own devising, they can discuss this with a supervisor.

In addition you may want to contact the School’s Honours Convenors, Associate Professor Gavin Pinniger for Physiology Honours and Associate Professor Jeremy Smith for Anatomy and Human Biology Honours. Neuroscience and Biomedical Science may also be accommodated.

Other useful websites include the School’s home page (http://www.aphb.uwa.edu.au/) and the Faculty’s honours page (http://www.science.uwa.edu.au/courses/honours).
# Brief Overview of APHB Honours Units (2015)

<table>
<thead>
<tr>
<th>Unit</th>
<th>Unit name</th>
<th>Tasks</th>
<th>Unit Mark</th>
<th>Final Mark</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Semester One</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APHB4001 6 Points</td>
<td>Research in Context – Literature Review</td>
<td>Project Plan</td>
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<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Literature Review</td>
<td>100</td>
<td>12.5</td>
</tr>
<tr>
<td>APHB4002 6 points</td>
<td>Research Design and Analysis</td>
<td>Ethics/Experimental design/Stats (Module assessments online)</td>
<td>20</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Experimental Design and Research Methodology</td>
<td>40</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proposal Seminar</td>
<td>40</td>
<td>5</td>
</tr>
<tr>
<td>APHB4003 6 Points</td>
<td>Advanced Experimental Techniques</td>
<td>Modules – Data management and statistical software and any 2 of: Animal care and husbandry / cell culture / Western Blot analysis / Histology / PCR / Immunohistochemistry / In Vitro physiological techniques / Field work / ....</td>
<td>25% per module</td>
<td>12.5</td>
</tr>
<tr>
<td><strong>Semester Two</strong></td>
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<tr>
<td>APHB4008 6 Points</td>
<td>Scientific Communication</td>
<td>Final Seminar</td>
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<td>Viva</td>
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<td>5</td>
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<tr>
<td>APHB4004/4005/4006/4007 24 Points</td>
<td>Research Project Part 1 &amp; 2</td>
<td>Dissertation</td>
<td>100</td>
<td>50</td>
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</tbody>
</table>

Student may opt to take two level 5 dissertation units in place of two level 4 ones. This will provide up to 48 points credit for students who successfully transfer to the Master of Biomedical Science at the completion of their Honours assessments. Student who actually take out their Honours degree will be eligible for up to 24 points credit if they then go on to study the Master of Biomedical Sciences or other Masters degrees. Note that no credit will be offered to students who take the Master of Clinical Audiology.
Information for Postgraduate Applicants

Masters by Coursework and Dissertation

The school offers two courses:

- Master of Anatomical Sciences
- Master of Human Biology

Both include a research dissertation similar to Honours and students will find this information useful to organise a supervisor and a project. Most students are sufficiently well prepared by these courses to proceed to a PhD, but it is not an automatic progression.

Masters by Research and Doctor of Philosophy (PhD)

These degrees are entirely research, and candidates have the opportunity to undertake larger, more complex projects. The Masters is two years full time or equivalent, and the PhD is usually 3 to 4 years. Candidates require previous research experience, usually an honours degree or Masters dissertation, but experience as a research assistant may be sufficient.

Candidates do not necessarily need to undertake their research in the same field as their previous study, so approach potential supervisors whose work interests.

http://www.science.uwa.edu.au/courses/postgrad/research

There are research student scholarships for both domestic and international students and candidates are encouraged to apply, however they are quite competitive. There are two rounds of offers each year. http://www.scholarships.uwa.edu.au/
Student Research Projects

Art in Science (SymbioticA)

Project outlines:
1. Art and science
2. Biological Arts (also known as bioart)
3. Cultural studies in Art & the Life Sciences

Project is suitable for Masters, PhD

Supervisor Dr Ionat Zurr

Essential qualifications
For Masters: BSc or BA. Applicants will be assessed on a case-by-case basis
For PhD: An appropriate Honours or Masters degree in Arts or Science or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

The Auditory Laboratory

Deafness and other hearing disorders such as tinnitus are among the most common forms of sensory impairment with profound consequences for the individual and society. Normal hearing depends on the proper function of the many components of the inner ear and the brain pathways to which it is connected. Our laboratory seeks an integrated understanding of the normal operation of this sense organ and its associated neural pathways and to describe the mechanisms underlying various hearing pathologies.

Project 1: Effects of repetitive transcranial magnetic stimulation on abnormal neural activity measured in an animal model for tinnitus.

With A/Prof Jenny Rodger

Tinnitus, or ringing in the ears, is a phantom auditory sensation arising from abnormal electrical activity that develops in the brain as a consequence of hearing loss. Repetitive transcranial magnetic stimulation (rTMS) can reduce tinnitus perception in human patients, with more sustained effects after longer duration regimes. In the project we will use an animal model of tinnitus in which we measure increased levels of spontaneous neural activity in the midbrain. We will investigate the effects of different stimulation regimes of rTMS on the abnormal central activity using neuroanatomical and electrophysiological techniques.
Project 2: Mechanism of the therapeutic effect of furosemide on tinnitus.

*With E/Prof Don Robertson*

Tinnitus, or ringing in the ears, is a phantom auditory sensation arising from abnormal electrical activity that develops in the brain as a consequence of hearing loss. In an animal model of hearing loss we have shown that acute treatment with furosemide can reduce the abnormal electrical activity as well as the tinnitus in animals within 8 weeks after hearing loss was evoked. This project will use this animal model of tinnitus to investigate the effects of chronic treatments with furosemide to study long-term effects of this drug on the abnormal electrical activity in the midbrain.

Project 3: Hidden hearing loss: neuropathy after noise exposures and relation to tinnitus

*With E/Prof Don Robertson*

There is now emerging evidence that the traditional indicator of hearing loss, changes in pure tone audiometric thresholds, fails to reveal important suprathreshold deficits linked to progressive cochlear nerve fibre degeneration after exposure to loud sounds. This project will investigate, in an animal model, electrophysiological evidence for loss of nerve fibres in cochlear regions that have fully recovered thresholds after noise exposure. Animals will also be tested behaviourally for evidence of tinnitus, in order to establish whether nerve fibre degeneration is linked to the onset of tinnitus and hyperacusis.

Project 4: Influence of the paraflocculus of the cerebellum on the auditory pathway.

*With E/Prof Don Robertson*

Tinnitus, or ringing in the ears, is a phantom auditory sensation arising from abnormal electrical activity that develops in the brain as a consequence of hearing loss. It has been shown that the paraflocculus of the cerebellum also shows abnormal activity after hearing loss and can affect the sensation of tinnitus. We want to investigate in an animal model of hearing loss the pathways between paraflocculus and different parts of the auditory pathway and investigate the effects of activation of the paraflocculus on activity in the auditory pathway. This project will use anatomical and electrophysiological techniques.

Project 5: Limbic system and tinnitus

*With Kristin Barry*

Phantom sensations are a curiously perplexing group of disorders. Tinnitus is a phantom sensation arising in the auditory system. Tinnitus has been commonly thought to be the result of abnormal neural activity in the auditory pathway. However, this doesn't account for why many people intermittently experience tinnitus. It has been proposed that the limbic system may exert an inhibitory gating effect on the abnormal neural activity in the auditory pathway. However, this has been minimally explored.

Our laboratory has recently shown that the nucleus accumbens can affect the auditory thalamus. The aim of this study is to find out if this effect is direct or indirect, via the thalamic reticular nucleus, as has been proposed in previous studies. This study will use electrophysiological recordings and histological techniques.

Project is suitable for: Honours, Masters, PhD

Supervisor: Assoc/Prof Helmy Mulders
Essential qualifications

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

Cancer and Cancer Targeted Therapies

Each project will take place in the Cancer Epigenetics Laboratory at the Perkins institute of Medical Research

Project 1. Epigenetic characterization of metastatic cells able to colonise and remodel the bone

With Dr. Fahimeh Falahi

Metastasis is a devastating problem in cancer and often the reason why tumor cells become resistant to treatment and kill the patient. Despite decades of study, little is known about the molecular basis as to why cells leave their niche, float into blood to reach other organs and colonize target organs. Recently, patient-specific blood circulating tumor cells (CTCs) have been isolated, which harbour a high degree of heterogeneity, as only a few cells are believed to successfully home to the target organs. Moreover, the study of these infrequent early events of colonization has been limited by our lack of model systems to image single CTCs. In patients, metastases are typically detected in late stages after the cells underwent often few years of dormancy and remain seeded but not seen. The aim is development of a 3D microengineered environment that would allow us to study at single cell resolution, the cellular, molecular, and epigenetic determinants of bone colonization of patient-derived CTCs.

Assoc/Prof Pilar Blancafort

Project 2. Engineering the cancer epigenome and targeting metastatic behaviour using CRISPR/Cas9

With Dr. Anabel Sorolla

Cancer is one of the major causes of death in Australia. For decades, the origin of cancer was attributed to genetic mutations. However, their involvement in gene regulation and cancer has illuminated the prospect of novel therapies. Epigenetic marks are heritable covalent modifications in the DNA or associated proteins. Epigenetic modifications provide the mechanisms by which a cell “knows” and “remembers” which genetic information to read and which to ignore. Epigenetic modifications include DNA methylation and modifications in the proteins that the DNA is wrapped around. Abnormal epigenetic modifications are frequently observed in cancer. In contrast to genetic mutations, epigenetic modifications are reversible and this can be used to restore the normal state of gene expression in the cancer. In this proposal, we aim to reverse the epigenetic modifications of key breast cancer drivers. We propose the development novel and more selective technologies able
to stably suppress the genes that cause breast cancer and breast cancer spread.


**Project 3. Development of a novel strategy using engineered peptides to selectively sensitis metastatic breast cancers to chemotherapy agents. With Dr. Anabel Sorolla**

This project focuses on generating novel targeted therapies for triple negative breast cancers. Triple negative breast cancers are responsible for most of the deaths related to breast cancer in Australia and in the world. These cancers do not express oestrogen receptor alpha, progesterone receptor and epidermal growth factor receptor 2, targets typically exploited in the clinic. They belong to the basal-like subtype breast cancer, comprising 15% of all breast cancers. In the metastatic setting they are highly resistant to chemotherapy. DNA-damaging agents used in chemotherapy, lacking target selectivity have generalized side effects. Thus, there is an urgent need to develop novel, more specific and targeted molecular approaches to treat this lethal disease.

Project is suitable for Honours, Masters, PhD

**Supervisor:** A/Prof Pilar Blancafort

**Essential qualifications**

For Honours: An appropriate undergraduate degree with a biological science, cell biology and basic molecular biology emphasis, and a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree with a biological, cellular and basic molecular biology science emphasis or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

**Desirable Skills/Experience**

Knowledge of statistics, cell biology, basic biochemistry and cell biology

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**Are paraspeckles involved in modulating stress-responses in pregnancy?**

It is well known that many different stressors influence gestational outcome, and that stress experienced in the womb may also influence development throughout life. Therefore there is an urgent need to better understand how stress is modulated within the uterine environment. Paraspeckles are subnuclear bodies that regulate gene expression in many cellular contexts, but particularly in response to cellular stress. Paraspeckles are a cellular structure that is built on a long noncoding RNA molecule, called NEAT1 (nuclear paraspeckle assembly transcript 1). This project will examine a role for paraspeckles in altering gene regulation in response to stress in pregnancy.

What is the evidence for a role for paraspeckles in placental response to stress?

(1) NEAT1 was originally named TncRNA, or trophoblast noncoding RNA, and trophoblasts are the cell type that form the placenta, but this has never been examined in terms of paraspeckles, (2) the NEAT1 knockout mouse has defects in female reproduction, and (3) paraspeckles are most prevalent...
in tissues that are highly plastic in their differentiation status, as well as highly secretory, both of which are typical to the placenta.

You will use RT-qPCR to measure NEAT1 RNA levels in murine placental tissue isolated from placentas of control and stress treated pups, as well as tissue staining methods to label paraspeckles in placental tissue. You will culture the BEWO trophoblast cell line, use microscopy to examine paraspeckle abundance in normal and stress conditions. Should time permit you will measure changes in abundance of paraspeckle target genes under stress conditions, as well as ablating paraspeckles by transfecting BEWO cells with siRNA targeting NEAT1 to characterise the effect of loss of paraspeckles in trophoblasts.

Project is suitable for Honours, Masters, PhD

Supervisor Archa Fox and Caitlin Wyrwoll

Essential qualifications

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis

Studying the molecular glue that holds paraspeckles together

Paraspeckles are subnuclear RNA-protein granules that regulate gene expression in many contexts, particularly under stress conditions. We are interested in studying the underlying properties of the forces that hold paraspeckles together. They are interesting structures, as they are not enclosed in a membrane – so how do molecules get targeted there, and how are these molecules held there? It is important to understand these processes as many of the molecules found within paraspeckles are also found in pathological toxic aggregates in neurodegenerative disorders, such as motor neuron disease. We need to understand the way these molecules functionally aggregate into structures such as paraspeckles, in order to figure out why they pathologically aggregate in neurodegeneration.

In this project you will use different molecular biology techniques to create mutations in key amino acids within different paraspeckle proteins, and then transflect fluorescent protein fusions of these constructs into cultured cells to examine their paraspeckle localisation. You will use fluorescent in situ hybridisation against the paraspeckle marker NEAT1 to detect paraspeckles. You will also work in vitro to study the biophysical properties of these proteins, in collaboration with Professor Charlie Bond.

This project will yield important insights into the nature of the functional aggregation of MND-associated proteins into paraspeckles.

Project is suitable for Honours, Masters, PhD

Supervisor Archa Fox and Caitlin Wyrwoll

Essential qualifications

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis
Currently, cardiovascular disease accounts for 32% of all deaths in Australia. This is a staggering proportion and continues to exceed death from all cancers combined (30%) and from road deaths (4%). A number of the deaths in the cardiovascular group are due to arrhythmia or disturbances in the electrical activity in the heart.

The normal electrical activity in the heart is controlled by the movement of ions through specialised channels in the membranes of cardiac cells. The autonomic nervous system plays an essential role in regulating cardiac function and many of its effects are mediated via sympathetic neurotransmitters that regulate the activity of these ion channels.

Certain pathophysiological conditions contribute to arrhythmias such as hypoxia and oxidative stress. Under these conditions there is a reduction in blood flow to the muscle in the heart resulting in a reduction in available oxygen and reactive oxygen species production. This is then followed by an increase in generation of reactive oxygen species. There is increased sympathetic drive and the heart has a greater vulnerability to sudden cardiac death. Understanding how cardiac ion channels are regulated under these conditions is crucial to understanding the ionic mechanisms involved in the triggering of ischemic arrhythmias. In addition an increase in reactive oxygen species can contribute to the development of cardiac hypertrophy (enlarged heart) and cardiac failure. We have good evidence that an early mechanism involves increased calcium influx through the L-type calcium channel.

The laboratory uses molecular biology techniques for expression and purification of ion channel protein and biochemical techniques for assay of generation of reactive oxygen species and cell viability. The method that will be used to study membrane currents is the patch-clamp technique. This technique is an extremely powerful method for studying the electrophysiological properties of biological membranes and its contribution to the advancement of research was justly recognised with the awarding of the Nobel Prize in Physiology or Medicine in 1991 to its developers Erwin Neher and Bert Sakmann. The technique can be used to study ion channels either at a whole-cell level or at the level of a single channel. In addition, since the intracellular composition of the cell can be controlled, this can be exploited to determine any second messengers involved. Patch-clamp technique is also used in the laboratory in conjunction with fluorescent dyes to record changes in intracellular calcium, reactive oxygen species generation and mitochondrial function.

**Project 1. How does the L-type calcium channel regulate mitochondrial function in pathology where actin filaments are disrupted?**

*Collaboration with Prof Christine Seidman, Harvard University and Prof Chris Semsarian, Sydney University*

Mitochondrial respiration is abnormal in hearts where actin or cytoskeletal proteins are disrupted and it is not understood why. This project follows from data generated by previous students in the lab. We have evidence that the L-type calcium channel can regulate mitochondrial function via the actin cytoskeleton. The project involves the use of patch clamp technique to study L-type calcium channel currents in mouse myocytes isolated from hearts of mice with disease involving disruption in cytoskeletal proteins and fluorescent detection of changes in mitochondrial membrane potential, NADH and superoxide production after activation of the channel. Alterations in expression of proteins in mdx mouse hearts that co-immunoprecipitate with the channel (assessed by Mass Spec) will be identified using immunoblot analysis.
**Project 2. How does oxidative stress alter the sensitivity of the L-type calcium channel to isoproterenol? What effect does this have on the action potential?**

*(Collaboration with Professor Yoram Rudy, University of Washington, St Louis, Missouri, USA)*

This question seeks to understand how arrhythmias occur during ischemia/reperfusion in the heart (after a heart attack). Isoproterenol is a beta-adrenergic agonist (and mimics the effects of catecholamines such as adrenaline in the heart). This project will use patch clamp technique to study the effect of oxidative stress and isoproterenol on L-type calcium channel currents in addition to K and Na channel currents and record changes in action potentials. Information gained from patch-clamp studies are incorporated into the Rudy-Luo model. Changes in action potential configuration are modelled and the relative risk of arrhythmia is determined.

**Supervisor** Professor Livia Hool

**Essential qualifications**

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

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**Cell Biology**

**Host and Viral Determinants of infection outcome.**

How does the interaction between host and virus influence Hepatitis C virus (HCV) and HIV infection outcome and disease progression? What are the genetic and immunological signatures of an effective host immune response against these viruses?

These questions will be addressed utilising samples from well-characterised local and international cohorts. Samples will be assayed using next-generation sequencing and single-cell technologies, and cellular immunology tests in a state of the art laboratory that houses robotic systems for high-throughput automation. The study outcomes will hopefully be used to inform vaccine design and future immune-therapy.

**Project is suitable for Honours, Masters, PhD**

**Supervisor** A/Prof Silvana Gaudieri

**Essential qualifications**

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.
Comparative Physiology of Adaptation

Our group is interested in the physiological mechanisms whereby animal species (including humans) adapt to environmental stressors. We focus mainly on thermal and osmotic stress, but exercise, inanition (starvation), and infection are also studied. Most experimental work is on systems level adaptations, but organ level adaptations are also studied. Our long-term aim is to identify specific adaptations that allow animals to survive and reproduce in challenging environments, and to identify how “homeostasis” handles the trade-offs when simultaneous challenges are presented to an organism, (such as combined thermal and osmotic stress, or combined inanition [starvation] and infection stress). Prospective Honours students with a background in General Systems Physiology, Exercise Physiology, Applied Animal Physiology, or Comparative Physiology are encouraged to apply. Depending on the project chosen a background in Cell Physiology could be an advantage.

Students will be exposed to a range of approaches and techniques including (in non-human animals) recovery anesthesia and surgery, implantation of physiological recording equipment, blood sampling for hormone measurement, and husbandry techniques for various species. In human research we use state of the art equipment to record physiological parameters in ambulatory subjects, including core and skin temperature transmitters, ambulatory blood pressure recording equipment, laser Doppler skin blood flow techniques, and infra-red thermography for surface temperature measurement.

Project 1. Ion channel expression in the hearts of thermoneutral and cold exposed mice
(With Prof Livia Hool, Cardiac Electrophysiology Lab, APHB)

The normal housing temperature for mice in most animal houses is below their thermoneutral zone, meaning that they are chronically cold exposed. Such exposure results in morphological and physiological changes, including larger body size, larger heart size, and elevated food intake and metabolism. During the light phase of the daily cycle, the resting heart rate (HR) of a mouse exposed to 30°C is about 375 beats/min. The resting HR increases by about 25 beats/min for every 1°C decrease in Ta below 30°C. When both arms of the autonomic nervous system are blocked, the heart beats at its intrinsic rate (i.e., the rate in a heart isolated from its nervous supply). Such autonomic blockade in a resting human results in an increase in HR because, at rest, parasympathetic tone dominates the control of the heart rhythm. At 22°C, the autonomic blockade of mice results in a decrease in HR, implying that the “resting” HR is sustained by elevated sympathetic tone. When mice are tested at 30°C, autonomic blockade results in an increase in HR because resting HR is dominated by parasympathetic input, just as it is in resting thermoneutral humans. The physiological demands on the heart are clearly impacted by exposure to cold. This project will investigate if changes in cardiac demand are associated with changes in the density or distribution of the ion channels that underlie heart function. Sub-projects may look at chronic versus acute cold exposure, or post-weaning versus pre-weaning exposure, or post-natal versus pre-natal exposure.
Project 2. Under nutrition and the defence of body temperature in the cold

The normal response of mammals to cold exposure involves peripheral vasoconstriction and an increase in metabolism. The former reduces heat loss from the skin while the latter increases heat production, helping to defend core body temperature. It is becoming clear that short term changes in energy (food) intake are detected by the body and that these signals have consequences for energy demanding activities like inflammation and reproduction. We would like to test whether these short-term signals also influence the energy demands for heat production during cold exposure. Human subjects will be exposed to cold while core and skin temperatures, as well as metabolic rate and skin blood flow are measured. Each subject will be exposed to the same cold stimulus twice, once while well fed and once after a period of reduced energy intake. The physiological responses will be compared.

Project 3. Does extracranial cooling really reduce brain temperature independently of arterial blood temperature?

It has become established in the last few years that cooling the brain reduces the long term effects of brain trauma such as stroke or ischemia. But the easiest way to cool the brain is to cool the body, and cooling the body creates problems of its own and can make the situation worse. The ideal treatment would be a means to cool the brain but leave the body at its usual temperature. That may sound easy but there is evidence that the main determinant of brain temperature is the temperature of the arterial blood reaching it. Despite this, many groups continue to test ‘extracranial selective brain cooling’ as a means to reduce brain temperature. We will use a rabbit model to look at brain – blood temperature coupling in several situations: during hypo- and hyper-capnia (which alter brain blood flow), and with ice packs applied to the cranium and a heater applied to the body. The data generated will provide good evidence for or against the possibility of brain – blood uncoupling. Techniques used will include an acute anesthetized rabbit preparation (like PHYL3002) with thermocouple measurement of temperatures. Students will be required to have done PHYL3002 and to have been an active participant in the techniques performed in the rabbit labs.

Project 4. Basal metabolic rate in mammals - How much does metabolism fall during anaesthesia?

(With Prof. Phil Withers and Dr Sean Tomlinson, Animal Biology)

The measurement of basal metabolic rate requires that an animal be rested, post-absorptive, awake, and within its thermoneutral zone. Measurements are made with an animal in a respirometry chamber (which measures metabolic rate by indirect calorimetry, the measurement of oxygen consumption and carbon dioxide production) and are usually made during the quiet-phase of the animal’s circadian cycle. These measurements are often confounded by animal movement and restlessness. Recent analyses indicate that the average small mammal has to remain in a chamber for 8 hours before a reliable estimate of BMR can be made. Some researchers have taken to lightly anesthetising animals before they place them into the metabolism chamber, which removes the confounding effect of animal restlessness. But to date no one has compared the awake BMR of small mammals to the anesthetised MR. During this project we will make measure both the awake BMR and the anesthetised MR of the same individuals, using mice and some other small mammals.

Project 5. A Role for Prostaglandins in the Vasodilator Skin Blood Flow Response to Heat Exposure and Exercise?

(With Prof Brian Dawson, Human Movement and Exercise Science)

When humans are placed in situations where enhanced heat loss is required to maintain thermal balance, skin blood flow increases. An elevation in skin blood flow is achieved by reduction of
vascular resistance in the skin. It is clear that central thermal input is important and leads to a reduction in vasoconstrictor tone and activation of a vasodilator system. For many years it was thought that the vasodilator system was mediated by Nitric Oxide, but subsequent study in humans has offered little support for NO mediation. The system seems to involve sympathetic cholinergic nerves, but the mediator is not Acetyl Choline. Attention has thus turned to Non-Adrenergic-Non-Cholinergic (NANC) mediators released from these nerves. In skeletal muscle prostaglandins and histamine have been implicated in ACh induced vasodilation, and so an involvement of these mediators in skin blood flow is possible. The project will involve exposing subjects to high ambient temperature (37°C) and light exercise, while core body temperature, skin blood flow, and skin temperatures are measured. Blood pressure and heart rate will also be recorded. Three experiments will be performed in random order 1) Control, 2) prostaglandin blockade, 3) histamine blockade. The results will have implications for sport and general medicine, because drugs that inhibit prostaglandins and histamine are freely available and they may be important in the etiology of heat illness.

Project 6. Vibration enhanced cooling of hyperthermic subjects

This project concerns the physiology of heat transfer. Exercise and heat exposure can lead to heat storage in the body and the state of hyperthermia. That state is associated with decrements in physical and mental performance, and can precipitate heat stroke, a medical emergency that can result in death. Strategies for cooling hyperthermic people involve methods to enhance heat transfer from the body to the environment, but can be hindered by the body's physiological responses to cold stimuli. For example, placing the body, or parts of it, into cold water causes a reduction in blood flow in the skin of the cooled area, while blood flow is critical for transferring heat from the body's core to the skin where it is lost to the environment. We recently showed that vibration as low frequency causes a vasodilation in the hands despite exposure to ice-water. The result was enhanced heat transfer and a faster decrease in core temperature. We would like now to test whether the response is specific to the hands, or whether whole body vibration can enhance skin blood flow in hyperthermic subjects exposed to cold air.

Projects are suitable for: Honours, Masters, PhD

Supervisor: Prof Shane Maloney

Essential qualifications

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

Evolutionary Ecology

The projects, which all have the same set of conditions, are:

- For highly motivated students there is potential to undertake field studies of family well-being in East Timor involving questions of family structure, ecology, social networks and
child growth. Some language study before commencing will be required.

- Intergenerational relationships in terms of help provided to adult offspring by mothers and fathers
- Family composition effects on development and reproductive strategies (survey work in Australia or work in Timor-Leste).
- Database development and statistical analyses of patterns of ecology and life history traits across species
- Behavioural studies of captive mammals (especially primates) at the Perth Zoo
- Behavioural studies of sex differences in humans

If you have another idea in the area of evolutionary ecology, talk to me about it; I am open to new and interesting questions.

**Suitable for:** Honours, masters, PhD

**Supervisor:** Associate Professor Debra Judge

**Essential qualifications**

For honours: An appropriate undergraduate major with a human biology, zoology or anthropology emphasis, and a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

For masters or PhD: An appropriate honours degree with a human biology, zoology or anthropology emphasis or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

**Desirable skills/experience**

Knowledge of basic statistical analyses is helpful but can be learned during the project. Ability to learn a further language is a requirement for some international research projects.

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**Ecology and Evolution**

**Project One: Primate behavioural ecology research:**

- Comparative study on aspects of primate socioecology (using literature data)
- Observational research on primate behaviour/cognition at the Perth Zoo

**Project Two: Human behavioural ecology**

Example: Questionnaire-based and experimental research on social networks, mate choice and fairness in humans

**Project is suitable for:** Honours/ Masters

**Supervisor Cyril Grueter**

**Desirable Skills/Experience**

Basic knowledge of statistics (especially regression analyses) would be desirable.
Education

Developing and Assessing Innovative Teaching Tools

These projects are suitable for students interested in entering a career in science communication and/or science education. They focus on creating virtual environments and educational animations for image intensive disciplines – coupled with modern pedagogy. An understanding of the histology of the human body would be useful – but not essential. No previous computing knowledge/skills is needed.

Book publishers must use images selectively as publishing in these disciplines becomes unacceptably expensive as more colour plates are used. In the e-learning environment, the full power of digital images is employed and the “picture is worth a thousand words” truism used to full effect to create more appealing and compelling learning environments students now demand.

I have developed an award winning learning system for image intensive disciplines that facilitates learning preferences of students consistent with their more intensive use of computers and the internet. I have demonstrated that creating virtual environments and animations and integrating explanatory content in the learning system provides extremely powerful learning tools that have a major impact on qualities of learning outcomes achieved by students accessing e-learning.

Based on this initial success there is an opportunity to create biological structures that can be studied within virtual environments whereby we are able to generate computer aided visualisation of microscopic structures in 3 dimensions with accompanying explanatory sound features and animations to simulate functions of structures presented. Research into the consequent educational values of these innovations then can be initiated.

Project is suitable for: Honours
Supervisor: Prof Geoffrey T. Meyer

Essential qualifications

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

Desirable skills/experience

An understanding of histology, but not essential.

New methods of teaching in Anatomy and Physiology

The nature of university teaching is changing radically. Increasing numbers of students, casualization of the teaching staff, development of new technology and software, socal media, changes in student behaviour and expectations all provide new challenges and opportunities. In UWA a radical overhaul of courses reflects some of these changes. A few prestigious US universities now provide free online
access to their lectures.

This project would involve the study of current teaching methods and the new student intake. Investigation of new technology, its usefulness and its impact on education (from mobile phones to Ipads, “clickers” 3D TV, virtual worlds, animations, plastination etc. etc.) It could involve the analysis of examination results for statistical correlations with examination methods, the development of new teaching material and the adaptation and assessment of new teaching methods in human anatomy.

**Project is suitable for Honours, Masters, PhD**

**Supervisor** Prof Stuart Bunt

**Essential qualifications**

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

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**Using a Virtual World for Teaching**

APHB In Second Life

I have a small grant to construct a virtual copy of the school of Anatomy, Physiology and Human Biology in the 3D world Second Life.

This is an experimental space in which to investigate the use of a 3D environment for the teaching of anatomy – which is all about 3D structures and the appreciation of 3D relationships.

The project would involve constructing 3D objects using cameras and software to import in to the virtual environment and working out how these could be used in science and preclinical education.

**Project is suitable for: Honours, Masters**

**Supervisor:** Prof Stuart Bunt

**Essential qualifications**

For Honours: Some second and/or third year units in human anatomy and physiology

For Masters: A biomedical/education background

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**Forensic Anatomy**

Please have a look at ircohe.net for lots more interesting info on who we are, what we do and the sorts of things you can do with our team. There is a link at the bottom of the home page especially for prospective 2015 projects.

**Have we got the scale right in fighting crime?**

Crime investigation relies on good science to make good decisions. The underpinning benchmarks of good science is good measurement with

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**Prof Marc Tennant**
known outcomes. We have a series of projects looking at building a strong science base under some of the methods of identification of victims of crime and disasters. Our team includes about 30 graduate students and more than 150 collaborators across the globe (ircohe.net). We collaborate with Forensic Science teams in Tasmania, Queensland and well as locally. The core values of the research team are about making a just and equitable society! All students are fully supported during their studies and we have a near 100% record of peer review publication from students’ efforts (with the student being the lead author). Research with this team will make a difference to the world.

**Project is suitable for** Honours, Masters, (extension of it will lead to Doctorate level).

**Supervisors:** Winthrop Professor Marc Tennant, Professor Estie Kruger
International Research Collaborative – Oral Health and Equity

**Assoc/Prof Estie Kruger**

**Essential qualifications**

For Honours: An undergraduate degree a minimum weighted average of about 65% in t level 3 subjects from an approved institution. Applicants will be assessed on a case-by-case basis.

**Desirable skills/experience**

A passion for understanding and addressing issues of justice. A little bit of basic computer skills. Ready to have a fun learning experience.

**Marginalised Communities**

Please have a look at [ircohe.net](http://ircohe.net) for lots more interesting info on who we are, what we do and the sorts of things you can do with our team. There is a link at the bottom of the home page especially for prospective 2015 projects.

We have a series of projects that address Australian marginalised communities and inequity. Below is a typical project but there are many others that are available to do – please if you have a passion in the area come and talk.

**Example Project: Do having grommets link to poor oral health?**

Many children suffer from ear infection and need to have grommets to treat the infections. The bacteria involved in these infections are similar to those that cause tooth decay. The proposed study will use Big Data techniques to test the hypothesis that there may be a linkage between these two conditions and that providing a dental surveillance program for patients attending for ear infections may reduce the emergency need for dental care for children and thus reduce health care costs and human suffering. The study will also include some health financing and cost-benefit analysis. Our team includes about 30 postgraduate students and more than 150 collaborators across the globe (ircohe.net). Our mission is to advance our understanding the issues of remote, rural and Indigenous peoples and access to good services. We have published on this in the world’s literature (about one paper every two weeks). The team has been together for over 15 years and we will support your efforts – we are a fun team! An international peer review publication will be expected to come from the research.

**Project is suitable for:** Honours, Masters, (extension of it will lead to Doctorate level).

**Supervisors:** Winthrop Professor Marc Tennant, Professor Estie Kruger & Professor Kate Dyson

International Research Collaborative – Oral Health and Equity

**Essential qualifications**
For Honours: An undergraduate degree a minimum weighted average of about 65% in the level 3 subjects from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

Desirable skills/experience

A passion for understanding and addressing issues of marginalized communities through better health systems. A little bit of basic computer skills.

International Communities

Please have a look at ircohe.net for lots more interesting info on who we are, what we do and the sorts of things you can do with our team. There is a link at the bottom of the home page especially for prospective 2015 projects.

We have a series of projects that address international community development. Below is a typical project but there are many others that are available to do – please if you have a passion in the area come and talk.

Example Project: Where are Health specialists in Sri Lanka?

Sri Lanka is a developing country about the size of Tasmania with the population of Australia with the history of 30 years long internal conflict which ended recently; leaving the people of Sri Lanka with many difficulties. Accessibility and affordability to quality health care is a serious issue among poor people in Sri Lanka compared to their Australian counterpart. This project will extend work already completed and published in the international literature (image to right). It will examine the distribution of specialist dental services and how people can get access to these services. Our team includes about 30 postgraduate students and more than 150 collaborators across the globe (ircohe.net). Our mission is to advance our understanding the issues of marginalised peoples and access to good services. We have published in this area in the world’s literature (about 1 paper every fortnight). The team has worked together for 15 years and will support your efforts – we are a fun team! An international peer review publication will be expected to come from the research, with the student as lead author.

Project is suitable for Honours, Masters, (extension of it will lead to Doctorate level).

Supervisors: Winthrop Professor Marc Tennant, Professor Estie Kruger, Dr Irosha Perera, International Research Collaborative – Oral Health and Equity ircohe.net

Essential qualifications

For Honours: An undergraduate degree a minimum weighted average of about 65% in the level 3 subjects from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

Desirable skills/experience

A passion for addressing issues of community marginalisation and addressing social justice is vital. A little bit of basic computer skills.
Functional Anatomy

1. Morphometrics.

Functional anatomy research involves understanding the meaning of shape variation in biology. The reason for the variation might be function, phylogeny/inheritance, environment, disease or just something that changes shape over time (like during growth or locomotion). The biological object is frequently a bone, but can be soft tissues (like faces, or feet!). Data can be collected from bone collections, or CT scans, photographs or living people. The questions that can be asked using these techniques have relevance to anatomy, biomechanics, development, evolution, forensics, medicine, physical anthropology, and palaeontology. The data collected can traditional linear measurements or 3D landmark data that is used in modern Geometric Morphometric analysis.

2. Finite element analysis.

Functional anatomy can also be explored using computer modelling of stress and strain in bones under different conditions. These methods have been used to test hypotheses about how muscles may sometimes act to reduce bending stress (and thus reduce the risk of bone breakage). This method can also be used to test hypotheses about why bones have particular shapes. For example why is the human femur curved? There must be some advantage to this curvature.

Examples of two projects that could be done in 2016:

1. The skulls in the Anatomy and Human Biology teaching collection are thought to have all come from South Asia. Data has already been collected on cranial collections from other parts of the world. This honours project could digitise the School's crania collection and analyse their variation in relation to known samples.

2. How does the 3rd trochanter work to relieve bending stress in the femur. Armadillos and their fossil relatives have a 3rd trochanter. The muscles that attach to the 3rd trochanter have been shown to relieve bending stress. But would it work as well if the trochanter was bigger or smaller, or more proximal or distal? This question could be explored using femoral models and finite elements analysis.

There are numerous other projects that could be negotiated. The possibilities are as wide as your imagination.

Supervisor Assoc/Prof. Nick Milne

Essential qualifications

For Honours: An appropriate undergraduate degree with a biological science emphasis, and a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree with a biological science emphasis or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.
Neuroscience

Cell and tissue transplantation, gene therapy and the repair of central nervous tissue damaged after injury.

The research by the neuroscience groups in Anatomy, Physiology and Human Biology has a particular emphasis on cell and tissue transplantation, gene therapy and the repair of central nervous tissue damaged after injury. Ways are being tested for preventing nerve cells from dying after injury and promoting the regenerative growth of damaged axons. The specificity of axon/target cell reconnection after injury is of particular interest. The potential for replacing compromised cells with new healthy cells, including stem cells, is also under investigation. Studies are mostly carried out in the visual system and in the spinal cord. Studies on visual system development are also a major interest of the Harvey lab.

Project is suitable for: Honours, Masters, PhD

Supervisor: Assoc/Prof. Stuart Hodgetts

Other supervisors: W/Prof Alan Harvey

Essential qualifications

For Honours: An appropriate undergraduate degree with a biological science emphasis, and a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree with a biological science emphasis or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

Desirable skills/experience

Neuroscience emphasis. Cellular and Molecular Biology would be helpful.

Physical MicroCT studies of vascularisation

(With Shane Maloney)

a) Taking advantage of the new high resolution scanner in CMCA in QEII we have been investigating the structure of the sheep rete, a complex network of capillaries below the brain used to cool the sheep’s brain under water stress. We wish to see how the efficiency of this structure varies between sheep and between sheep strains to identify the best heat adapted sheep, suitable for the Australian climate.

b) Blood supply of the nasal cavities, this is one of the last areas of human anatomy yet to be understood. Nose bleeds are a common, and usually innocuous, occurrence. However, as nasal vessels are embedded in the nasal conchae they may be unable to contract after damage and exanguination has occurred following epistaxis. This area is notoriously difficult to dissect. This project would involve injection of iodine into the facial and

Assoc/Prof Stuart Hodgetts

Prof Alan Harvey

Prof Stuart Bunt
maxillary arteries followed by use of the microCT to produce high resolution angiograms of the nasal vasculature.

Project is suitable for Honours, Master, PhD
Supervisor Prof Stuart Bunt
Essential qualifications
For Honours: Some second and/or third year units in human anatomy and physiology
For Masters or PhD: Anatomy and physiology background

Physical properties of nervous tissue
Working with Karol Miller’s large research group in Mechanical engineering we are looking at various physical aspects of brain structure such as its elasticity, fluid permeability, and resistance to compression. These measurements are then used to model brain deformation in surgery and disease. Accurate modelling of brain movement during, for example, robotic guided surgery is necessary to ensure that electrodes or excisions are accurately placed in tumours or selected brain nuclei. Knowledge of the interface between the skull and brain define the edge effects of brain distortion in impact injuries. We are also interested in fluid flow through brain tissue as this can effect properties such as rigidity in the enclosed skull and responses to distortion of the brain ventricles by space filling lesions such as tumours and blood clots. The research will involve experimenting on sheep and human brain tissue, applying stresses and strains in finely calibrated apparatus to obtain the required parameters. For fluid flow we wish to investigate mass flow using gold nano particles followed by electron microscopy to study microflow in brain tissue

Project is suitable for Honours, Master, PhD
Supervisor Prof Stuart Bunt
Essential qualifications
For Honours: ANHB2217 preferred (other neuro units may suffice).
For Masters or PhD: A background in biology with some neuroanatomy/neuroscience

The Brain Bioengineering and Imagining
I have been working for some time with Karol Miller’s group in Engineering. This group is interested in modelling the deformation and movement of the brain in injury and during surgery. To do this modelling they need to know various parameters about the brain, e.g. how compressible it is, how fast liquid can travel through brain tissue, how elastic it is etc. etc. Surprisingly many of these basic brain structural parameters are not know with any certainty.

This research would involve constructing apparatus, sometimes with the help of engineers to test and measure these parameters in post mortem brain tissue, usually from sheep. We are also interested in imaging the brain and comparing the results from MRI/CT/ultrasound etc. to theoretical modelling results. The engineers are good at constructing models of brain deformation but know little anatomy so will need your help in comparing the results.

Project is suitable for: Honours, Master, PhD
Supervisor Prof Stuart Bunt
Essential qualifications
For Honours: An appropriate undergraduate degree with a biological science emphasis, and a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree with a biological science emphasis or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

**Fibre Pathways after Spinal Cord Regeneration**

Unlike humans and other mammals, fish can regenerate their spinal cords. This gives us the ability to examine what may happen when the mammalian researches eventually get good spinal cord regeneration in mammals. Will the new axons make appropriate connections, will they get lost in scar tissue?

This experiment would involve severing the spinal cord of fish while they are anaesthetized, allowing the cord to regenerate, then labelling sub sets of axons with fibre tracers to examine where the regenerated axons have grown. The spinal cords would then be examined.

**Project is suitable for:** Honours, Master, PhD

**Supervisor:** Prof Stuart Bunt

**Essential qualifications**

For Honours: An appropriate undergraduate degree with a biological science emphasis, and a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree with a biological science emphasis or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

**The role of kisspeptin in energy expenditure in the mouse**

Recent data from our laboratory demonstrate no effect of central kisspeptin treatment on accumulative food intake. Despite this, neuroanatomical links have been established between kisspeptin cells and appetite regulating neurons expressing neuropeptide Y (NPY) and Pro-opiomelanocortin (POMC). Moreover, kisspeptin results in the activation of NPY cells in the hypothalamus. Electrophysiological data also suggests kisspeptin regulates the activity of NPY, and also POMC neurons. Taken together, these data strongly suggest kisspeptin has effects on energy expenditure.

Experiments will be conducted to measure the effect of kisspeptin and the absence of kisspeptin signalling in mice on energy Expenditure. GPR54 (Kiss1r) knock-out mice or their wild-type littermates will be challenged with a high fat diet for 12 weeks. Mice will then be tested on indices of energy balance including:

- Measurement of whole body energy metabolism (using metabolic cages for indirect calorimetry)
- Assessment of whole body glucose metabolism (using intraperitoneal glucose and insulin tolerance tests)
• Assessment of body composition (Using dual energy X-ray absorptiometry DEXA)
• Assessment of neuropeptide systems involved in energy metabolism (using in situ hybridisation).

Results from these experiments will shed light on the known link between the reproductive system and metabolism and will, potentially, offer novel therapeutic alternatives for the treatment of obesity and related metabolic disorders.

Project is suitable for: Honours, Masters, PhD
Supervisor: Dr Jeremy Smith

Essential qualifications: none

Desirable skills/experience: A background in molecular biology is desirable but not essential.

The role of kisspeptin in implantation and placentation

Kisspeptin, the neuropeptide product of the Kiss1 gene, is synthesized by neurons within the hypothalamus and is critical for the release of gonadotrophin-releasing hormone (GnRH) and fertility. In humans, kisspeptin secretion into the peripheral circulation increases dramatically (approximately ten-thousand-fold) during pregnancy and declines precipitously at term, indicating a placental origin. The placenta is known to express KISS1 and kisspeptin receptor (KISS1R) mRNA and it appears to be localized to the trophoblast compartment. We aim to determine the expression of Kiss1 mRNA in the mouse placenta and examine the effect of reduced kisspeptin signaling (using a kisspeptin receptor knock-out mouse) on feto-placental growth.

Experiments will be conducted to measure feto-placental growth in an Kiss1r KO model.

Kiss1rKO mice or their wild-type littermates will be examined at day 14 and 18 of pregnancy.

We will examine:
• Fetal weight
• Placental weight and morphology
• Assessment of key placental genes (using RT-PCR)
• The effect of kisspeptin and the absence of kisspeptin signalling in mice on placental histology

Results from these experiments will shed light on the function of kisspeptin in the placenta and will, potentially, offer novel therapeutic alternatives for the treatment of placental insufficiency and/or pre-eclampsia.

Project is suitable for Honours, Masters, PhD
Supervisors Dr Jeremy Smith and Asst/Prof Caitlin Wyrwoll

Desirable skills/experience
A background in molecular biology is desirable but not essential.
Neonatal Physiology and Biology

Postnatal Steroids and Antenatal Chorioamnionitis in the Ventilated Preterm Lamb – Short Term Outcomes

Mechanical ventilation induces a local inflammatory response that prolongs the need for mechanical support and increases the risk of systemic infection and inflammation: Duration of mechanical ventilation is an independent risk factor for complications of prematurity including bronchopulmonary dysplasia (BPD) and adverse neurodevelopmental outcomes. Postnatal corticosteroids are given to rescue infants with severe respiratory disease but may also impair neurodevelopmental outcomes. There is a growing awareness that individual patient disease profile, such as a pre-existing pro-inflammatory state may modify the risk of adverse outcomes. For example, the fetus exposed to inflammation has an increased risk of ventilation related brain injury and development of chronic lung disease. It is unknown how postnatal steroid treatment modulate these risks.

This project is offered within the newly established Preclinical Intensive Care Research Unit (PICRU) and offers multiple Honours and PhD student opportunities investigating the impact of mechanical ventilation, inflammation and steroids on the major organs of interest (brain, heart & lungs), or other organ systems including the airways, immune system, gastrointestinal system, eyes, kidneys and gonads amongst others. Projects may have a functional physiology (in vivo and/or in vitro), or more laboratory (molecular & cell biology) focus depending on the interests of the student and the time available for investigation.

Most of the tissues for this project were collected in 2015, therefore Honours projects for 2016 would focus on tissue analysis. Projects suitable for Honours are available in one or more of the following groups of investigations, according to student interest.

- Neuroimaging – hemispheres of brain are preserved in paraformaldehyde reading for 9.4 T magnetic resonance imaging (MRI) to assess the impact of antenatal chorioamnionitis and postnatal steroids on volumes and neural connections (via tractography)
- Ocular vascular development/immunology and evidence of pro-inflammatory changes that may precede development of retinopathy of prematurity (Prof Jane Pillow/Prof Maria Degli-Espoti, Lions Eye Institute)
- Effect of chorioamnionitis and postnatal glucocorticoid exposures on
  i. developmental gene expression in the lung (molecular project)
  ii. pulmonary inflammation (histological/immunohistochemistry/ELISA)
  iii. ileal and jejunal mucosal integrity and maturation
  iv. systemic inflammatory responses
  v. neurological inflammation, injury & apoptosis:

Students will be able to access additional training and development opportunities through the NHMRC Centre for Research Excellence in Improving the Immediate & Longer-Term Outcomes of Preterm Infants (2013-8). The major costs of the project are funded by an NHMRC Research Project Grant

Project is suitable for: Honours/ Masters/PhD
Supervisor: Professor Jane Pillow
Additional supervisors will be involved depending on the student interests and organ system to be studied

**Essential qualifications**

**For Honours:** An appropriate undergraduate degree with a biological science emphasis, and a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

**For Masters or PhD:** An appropriate Honours degree with a biological science emphasis or equivalent research experience from an approved institution. Applicants are assessed on a case-by-case basis.

**Desirable skills/experience**
Preparedness to work with large animals
Strong work ethic

**Postnatal Steroids in the Ventilated Preterm Lamb – Long Term Outcomes**

Mechanical ventilation induces a local inflammatory response that prolongs the need for mechanical support and increases the risk of systemic infection and inflammation: Duration of mechanical ventilation is an independent risk factor for complications of prematurity including bronchopulmonary dysplasia (BPD) and adverse neurodevelopmental outcomes. Postnatal corticosteroids are given to rescue infants with severe respiratory disease but may also impair neurodevelopmental outcomes. There is a growing awareness that individual patient disease profile, such as a pro-inflammatory state may modify the risk of adverse outcomes. It is unknown how postnatal steroid treatment modulate these risks.

This project is offered within the newly established Preclinical Intensive Care Research Unit (PICRU) and offers multiple Honours and PhD student opportunities investigating the impact of mechanical ventilation, inflammation and steroids on the major organs of interest (brain, heart & lungs), or other organ systems including the airways, immune system, gastrointestinal system, eyes, kidneys and gonads amongst others. Projects may have a functional physiology *(in vivo and/or in vitro)*, or more laboratory (molecular & cell biology) focus depending on the interests of the student and the time available for investigation.

Lamb studies for this project will extend from Oct 2015 until November 2016. Some groups may be complete by August 2016. Lambs will be studied until 4 months of age, hence studies requiring access to tissues are only suitable for PhD students or Honours projects commencing mid-year.

Honours projects will relate primarily to functional/physiological studies permitting involvement of Honours as well as PhD students.

**Functional Assessments (suitable for Honours or as part of a PhD) will include:**

- Neuroimaging – MRI studies on preterm lambs at 2-4 weeks corrected postnatal age to assess cerebral vascular networks, brain volumes and tractography
Imaging of ocular vascular development relevant to retinopathy of prematurity using RETCam, optical coherence tomography and fluorescent ophthalmoscopy (Prof Jane Pillow/Prof Maria Degli-Espoti, Lions Eye Institute)

Comparison of ventilator requirements and assessments of shunt/shift derangements (Prof Jane Pillow)

Longitudinal measurements of lung volume and ventilation inhomogeneity and oscillatory mechanics (Prof Jane Pillow/Prof Raffaele Dellaca - Italy)

Respiratory polysomnography/control of breathing (Assoc Prof Jane Pillow / Prof Raffaele Dellaca – Italy)

Neurodevelopmental assessments of memory, executive function, motor activity, stress-responses (Assoc/Prof Dominique Blache)

Echocardiographic function (Prof Jane Pillow/Clin Assoc Prof Andy Gill)

Immunological development/innate & adaptive immunity (Prof Jane Pillow/Dr Andrew Currie)

Neurobehavioural and neurodevelopmental function including assessment of emotion/temperament, movement/gait, neuroendocrine responses to stress, memory and executive function

A wide range of options also exist for tissue assessments as for the previous project. Students are encouraged to discuss their specific area of interest with the Project Co-ordinator – Prof Jane Pillow

Students will be able to access additional training and development opportunities through the NHMRC Centre for Research Excellence in Improving the Immediate & Longer-Term Outcomes of Preterm Infants (2013-8). The major costs of the project are funded by an NHMRC Research Project Grant

**Project is suitable for:** Honours/PhD

**Supervisor:** Professor Jane Pillow

Additional supervisors will be involved depending on the student interests and organ system to be studied

**Essential qualifications**

**For Honours:** An appropriate undergraduate degree with a biological science emphasis, and a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

**For Masters or PhD:** An appropriate Honours degree with a biological science emphasis or equivalent research experience from an approved institution. Applicants are assessed on a case-by-case basis.

**Desirable skills/experience**

Preparedness to work with large animals
Absorption of Colostrum from the Gastrointestinal Tract in the Preterm Lamb

Project Outline

Colostrum is a nutrient and immunoglobulin rich fluid produced by the ewe shortly before parturition. Colostrum is a rich source of energy, facilitating homeostasis and immediate survival after birth. Also, the maternally derived antibodies are critical to help lambs fight off infection whilst they build their own stable immune system. Lambs are also critically reliant on the absorption of colostrum from the gastrointestinal tract in the first 24 hours after birth for protection against infection.

The premature subject will have an immature gastrointestinal system at birth. It is unclear whether preterm lambs are able to absorb colostrum from the gastrointestinal tract as efficiently as the more mature term lamb.

Further, the nutritional composition and immunoglobulin content of the colostrum produced by the ewe giving birth prior to full gestation is unknown.

The project aims to evaluate the increase in plasma immunoglobulin level over the 48 hours after birth in term lambs and preterm lambs of different gestations and to analyse samples of colostrum for potential nutritional and immunological benefit. The information will assist future management of preterm lambs in the PICRU.

Students will be able to access additional training and development opportunities through the NHMRC Centre for Research Excellence in Improving the Immediate & Longer-Term Outcomes of Preterm Infants (2013-8). The major costs of the project are funded by an NHMRC Research Project Grant

Project is suitable for: Honours

Supervisor: Professor Jane Pillow

Additional supervisors will be involved depending on the student interests and organ system to be studied

Essential qualifications

For Honours: An appropriate undergraduate degree with a biological science emphasis, and a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

Desirable skills/experience

Preparedness to work with large animals
Optimising early life environment for long term health outcomes

Research interests in my lab focus on the importance of the early life environment for placental and fetal development and consequent adult health outcomes of the offspring. Of particular interest is the role that stress hormones (glucocorticoids), maternal under-nutrition and maternal vitamin D deficiency have in influencing placental and fetal development.

Project topics can include:

- Impact of early life environment on placental and fetal organ vascularity
- The significance of placental blood flow for fetal heart development
- Ramifications of vitamin D deficiency on neurodevelopment

Feel free to contact Caitlin Wyrwoll to discuss any other Reproductive Biology topics they may wish to pursue.

Project is suitable for Honours, Masters, PhD

Supervisors Asst/Prof Caitlin Wyrwoll

Essential qualifications

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

Desirable skills/experience

A background in molecular biology is desirable but not essential.

Reproductive and Developmental Biology

The major interests of our group centre on the importance of circadian biology in relation to placental function, maternal adaptation to pregnancy, and developmental programming. Current studies are focussed on the impact of maternal obesity, omega-3 fatty acids and glucocorticoid excess on pregnancy outcome (from the perspective of both the mother and the developing fetus).

Project 1: Developmental origins of health and disease (DOHAD)

Studies in relation to DOHAD focus on the effects of fetal glucocorticoid excess on the adult phenotype, particularly in relation to programming of adult-onset diseases such as hypertension, diabetes and obesity. The capacity of postnatal diets to either exacerbate (e.g. by a high fat diet) or rescue (e.g. dietary fish oil) adverse outcomes is an important focus of this work.

Tissue banks have been collected from a large scale glucocorticoid programming study and these are available for analysis. Tissues including heart, kidney and adrenal gland have been collected at 6
months of age from control and programmed offspring raised on standard, high fat or high fat/high omega-3 diets. They have been collected at four time points across a 24 hour period, enabling circadian profiling of gene expression and tissue function to be layered into the analysis.

Project 2: Circadian rhythms in the spiny mouse placenta (Chief Supervisor Dr Peter Mark, with W/Prof Brendan Waddell and Dr Hayley Dickinson, Monash University)

Circadian biology underpins all major metabolic processes to appropriately align physiology of the organism with behaviour. Altricial (immature at birth) organisms, such as the rat and mouse, have minimal circadian variation in placental function, possibly to supply the fetus with constant nutrition during the relatively brief period of fetal growth. Precocial (relatively mature at birth) organisms are often born with metabolic rhythmicity (e.g. in liver function) which may be driven by exposure to peaks and troughs in substrate supply from the placenta.

This project aims to determine whether placentas from the precocial spiny mouse exhibit distinct circadian rhythmicity in their function in association with fetal liver rhythmicity. Samples have been collected from pregnant spiny mice in collaboration with Dr Hayley Dickinson, The Ritchie Centre at The Hudson Institute, Victoria. Placental expression of clock genes and nutrient transporters will be determined at various stages throughout gestation to determine the timing of onset for placental rhythmicity.

Project is suitable for Honours, Masters by Coursework, Masters by Research, PhD

Supervisor Dr Peter Mark and Prof Brendan Waddell

Essential qualifications

For Honours or Masters: An appropriate undergraduate degree with a biological science emphasis, and a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters by Research of PhD: An appropriate Honours degree with a biological science emphasis or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

Reproductive Biology

Lifestyle and psychosocial factors influencing human fecundity and fertility (database and survey studies)

- The impact and interaction of age, nutrition, and stress on male and female reproductive processes (database, survey and lab based projects possible).
- Issues surrounding the use of donated gametes and embryos in assisted reproductive technology (survey based and qualitative type projects possible).

For students interested in assisted reproductive technology, opportunities exist for collaborative projects in the above areas with Dr Peter Burton at Concept Fertility Centre.
Students are encouraged to contact Kathy Sanders to discuss any other topics on Reproductive Biology they may wish to pursue.

Project is suitable for: Honours, Masters, PhD

Supervisor: Dr Kathy Sanders

Essential qualifications:

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

Respiratory Physiology

The respiratory group in APHB has had a long-standing interest in the control and function of conducting bronchi. The trachea, bronchi and other airways conduct air into and out of the lung. During an asthma attack contraction of airway smooth muscle (ASM) narrows the conducting bronchi and obstructs airflow. Airway obstruction also occurs in several other respiratory disease including Chronic Obstructive Pulmonary Disease (COPD), chronic bronchitis and emphysema. The focus of our research has been in understanding the detailed mechanisms involved in the control of airway diameter and airway obstruction.

Project 1 Airway wall isotropy: is a push the same as a pull?

Airway narrowing, bronchoconstriction, is a key feature of several respiratory diseases including asthma. Our developing understanding of bronchoconstriction now suggest that narrowing is dependent on the interactions of airways smooth muscle contraction with the loads placed on the airway and the modulating actions of breathing movements such as deep breaths. Current models of airway function assume that the airway is isotropic and behaves the same way to forces pulling on the outside as to a pressure in the lumen pushing from the inside. This project aims to directly test that assumption using Anatomical Optical Coherence Tomography (aOCT) in airways isolated from pig lungs. These experiment use state of the art imaging techniques being developed at UWA’s school of electronic and electrical engineering to map the inside of individual bronchi with LASER probes. The question is how does the lumen move in response to an inflation by positive pressure in the lumen compared to negative pressure on the serosal surface and what change does that produce during airway contraction and in simulated breathing movements. This project uses isolated lung tissue from pigs.

Supervisors: Assoc Lecturer Peter McFawn, Asst/Prof Peter Noble

Dr Peter McFawn

Dr Peter Noble
Project 2 Respiratory pattern in airway disease

Over the last decade a surprising finding in respiratory research is that breathing protects against airway obstruction in healthy subjects but not in subjects with asthma or COPD (chronic obstructive pulmonary disease). In a healthy person taking a deep breath greatly reduces bronchoconstriction and relaxes airway smooth muscle. Few studies have examined the pattern of breathing and how this differs between healthy subjects and those with respiratory disease. This project aims to measure the frequency and pattern of spontaneous deep breaths (i.e. sighs) in healthy subjects and patients with respiratory disease such as asthma. A collaborative project involving APHB at UWA and Respiratory Medicine at QEII that will use respiratory monitors to measure normal breathing pattern in human volunteers.

Supervisors: Assoc Lecturer Peter McFawn, Asst/Prof Peter Noble

Project 3 Force adaptation

Over the last decade work with isolated airway smooth muscle (ASM) has shown that ASM has a plastic length-tension curve, that is given time the muscle will adapt to make its current length the optimum operating length. Two recent reports in the literature suggest a similar phenomenon can happen to muscle force production, where ASM is left partially contracted for some time the maximum force that can be generated is increased. This project will attempt to prove the phenomena of force adaptation and test whether continuous partial contraction can cause an asthma-like phenotype. This project will use bronchial segments from large animal species (sheep and pigs) and also involve translational experiments on human airway tissue.

Supervisors: Assoc Lecturer Peter McFawn, Asst/Prof Peter Noble

Project 4 Airway Structure in Disease

In airway diseases such as asthma and chronic obstructive pulmonary, disease remodelling of the airway wall occurs. That is, the wall becomes thicker with more muscle and more connective tissue. But does the greater thickness of muscle mean more contractile filaments in the muscle or is it mostly “empty space”? The aim of this project is to use immunohistochemistry to assess the actin and myosin in the smooth muscle cells. Airway and lung tissue samples from asthmatic, COPD and control patients will be used to determine if the increased muscle mass also means more contractile filaments. This project would run as a collaboration involving APHB at UWA and Respiratory Medicine at QEII.

Supervisors: Assoc Lecturer Peter McFawn, Asst/Prof Peter Noble

Project 5 Novel Airway Explants

Cell culture is an extremely useful technique but limited for studying integrated organ function like a bronchus. The tissue explant technique is an adaptation of tissue culture to larger structures like an intact blood vessel or airway tube. Explanting allows prolonged incubation of an isolated tissue under highly controlled conditions that is not possible in vivo or in classical organ bath methods. Our question is how do changes in the mechanical and chemical environment of the lung produce airway wall structural changes? Can incubation of tissues with cytokines present in asthma make an airway “asthmatic” or does prolonged exposure to high intraluminal pressure change airway contractility? This project would involve developing a method to explant bronchi from large animal species (pigs and sheep) under conditions were the luminal pressure can be controlled.

Supervisors: Assoc Lecturer Peter McFawn, Asst/Prof Peter Noble
Project 6 **Variable breathing and airway function**

Our laboratory has previously shown that simulated breathing movements in isolated bronchial tubes prevents airway collapse. It is theorised that a loss of the beneficial effects of breathing is a precursor to airway obstruction in asthma. However, while our prior studies have modelled breathing as a fixed sinusoidal rhythm, breathing is irregular in nature comprising both small and large breaths at a variable rate. There is now increasing evidence to suggest that this natural irregularity of breathing promotes normal airway function but this has yet to be tested. The present project will for the first time determine how a variable breathing rhythm impacts airway function and how this may be disrupted in disease leading to poor airway function. Techniques will include a newly developed and custom-designed organ bath system that provides a comprehensive assessment of mechanical airway wall properties and simulation of different human breathing rhythms.

**Supervisors:** Assoc Lecturer Peter McFawn, Asst/Prof Peter Noble

Project 7 **A contemporary mouse model of lung disease**

A new paradigm in respiratory disease is that structural and physiological abnormalities may arise independent of inflammatory pathways. We have established a mouse model that overexpresses transforming growth factor alpha (TGFalpha), producing lung remodeling particularly when the Early growth response 1 (Egr-1) gene is ‘knocked out’. Importantly, these changes are mediated in the absence of inflammation. We are interested in the functional and structural consequences of TGFalpha induced respiratory disease including airway remodeling and smooth muscle contractility, lung stiffening and diaphragmatic function. The data generated is relevant to asthma, chronic obstructive pulmonary disease, pulmonary fibrosis and other respiratory disorders. While the project makes use of a sophisticated transgenic and knock out mouse model, our focus is on lung physiology and is suitable for any student interested in airway-structure function relationships. Techniques include, in vivo assessment in mechanically ventilated and anaesthetised mice, organ bath experiments on isolated mouse trachea, bronchi or diaphragm muscle, and stereological assessment of tissue (“stereology” – the unbiased assessment of structure).

**Project is suitable for Honours, Master, PhD**

**Essential qualifications**

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.
Evaluating skeletal muscle performance in mouse models of disease and superior athleticism

Skeletal muscle comprises up to 40% of a human’s body mass and is crucial for every day actions such as breathing, moving and swallowing. When skeletal muscles do not function properly they can cause severe diseases, such as muscular dystrophy and congenital myopathy. An emerging skeletal muscle disease associated with ageing is sarcopenia, which is tightly linked to osteoporosis and falls in the elderly.

Having the ability to study animal models is often crucial for medical researchers to better understand biology, and to then devise and evaluate potential therapies for disease. Even if certain experiments can be performed in tissue culture, ultimately studies require an animal model to be the test-bed to allow appropriate and thorough evaluation.

We have previously successfully studied the skeletal muscle physiology of a range of mouse models. We currently have a range of mouse lines that have skeletal muscles that are either impaired or superior in function. For those that are impaired, where mice have an inability to exercise normally, the aim is to understand why this impairment exists, and whether the application of possible treatments is efficacious. In those mouse lines with skeletal muscles that are performing better than expected (e.g. mice show an exceptionally high capacity to exercise), we would like to unravel the underlying mechanisms responsible. Once uncovered, activation of these mechanisms could be used in the future to prevent or treat skeletal muscle diseases such as muscular dystrophy.

In addition to skeletal muscle physiology techniques, students would have the opportunity to include other techniques used to phenotype mice in their tailored Honours project. These include genetics and molecular biology, tissue biopsy and histology, immunostaining, various types of microscopy, protein and RNA extraction, voluntary running wheel analysis, and magnetic resonance imaging.

Please contact us to discuss the possible projects on offer if you are inspired to try to better understand skeletal muscle diseases and to develop therapies for them. If you choose such a project, you would use a range of exciting techniques with well-established, respected and friendly medical researchers at the School of Anatomy, Physiology and Human Biology, and at the Harry Perkins Institute of Medical Research.

Project is suitable for Honours, Masters, PhD

Supervisor Assoc/Prof Tony Bakker

Other Supervisor: Assoc/Prof Kristen Nowak

Essential qualifications

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.
Can blocking skeletal muscle stretch-activated Ca\(^{2+}\) channels prevent ventilation-induced diaphragm skeletal muscle damage.

Preterm babies are often unable to breathe on their own due to the immaturity of the respiratory system, and require an extended period of mechanical ventilation. While essential for survival, this intervention is thought to lead to damage of the developing respiratory muscles, which can significantly extended the requirement for ventilation and also contribute to respiratory failure.

We have recently shown that diaphragm muscle from preterm lambs is more susceptible to stretch-induced muscle damage than diaphragm muscle from lambs born after the normal gestation period. Skeletal muscle fibres contain specialised stretch-activated Ca\(^{2+}\) channels, which are thought to play a role in muscle development and growth. However when they are inappropriately or over activated, muscle damage can result through intracellular Ca\(^{2+}\) overload and activation of Ca\(^{2+}\)-activated proteases and the release of reactive oxygen species.

Stretch-activated Ca\(^{2+}\) channels can be blocked by the antibiotic streptomycin, and this drug has been used to prevent stretch-induced muscle damage in animal models of Duchenne muscular dystrophy (Zhang et al., 2012). We hypothesise that stretch of the diaphragm during artificial ventilation activates stretch-activated Ca\(^{2+}\) channels leading to muscle damage and dysfunction.

**Aims of the study:**

**Aim 1.** To compare the effects of passive stretch and lengthening (eccentric) contractions on force output in diaphragm preparations from young (3 weeks old) and mature mice (8 weeks) using a muscle test system. These experiments will determine whether young mice are more susceptible to stretch induced diaphragm damage.

**Aim 2.** To investigate the ability of streptomycin to prevent stretch-induced muscle damage in diaphragm preparations from young and mature mice.

**Aim 3.** To determine whether mechanical ventilation results in diaphragm muscle damage using a mouse artificial ventilation model.

**Aim 4.** To examine whether any ventilation-induced diaphragm damage can be prevented in mice by pre-exposure to streptomycin.

The results of this study could provide new strategies to prevent ventilator-induced diaphragm dysfunction in premature babies.

**References**


**Project is suitable for Honours, Masters, PhD**

**Supervisor** Assoc/Prof Tony Bakker

**Essential qualifications**

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.
Skeletal Muscle Physiology

Skeletal muscles serve numerous functions that are essential for life. Not only do they provide the power required for movement and locomotion, but they also have vital roles in respiration, thermoregulation and metabolism. Not surprisingly, the loss of muscle mass and/or muscle function can be life threatening. Skeletal muscles of pre-term babies, elderly people and of people suffering from muscle diseases such as the debilitating Duchenne muscular dystrophy (DMD) are highly vulnerable to injury and are inherently weaker than healthy muscle. The goal of our research group is to understand the mechanisms of muscle damage and contractile dysfunction associated with ageing and disease and to evaluate potential therapeutic treatments to alleviate the severity of symptoms and improve the quality of life of these individuals.

Using a range of experimental models from in vitro single cell recordings to in vivo experiments on whole animals we investigate the molecular processes regulating muscle contraction and the mechanisms of contractile dysfunction from a cellular and systems approach. Students will be exposed to experimental techniques including recovery anaesthesia and surgery, microdissection of whole muscle and single muscle fibres, cell-culture and calcium imaging. We have several multidisciplinary collaborations with local and international researches and are particularly interested in:

i) Factors that affect diaphragm function and contribute to breathing problems in pre-term infants;

ii) Unravelling the molecular processes of force enhancement in skeletal muscle;

iii) Evaluating therapeutic treatments for Duchenne muscular dystrophy; and

Specific details of Skeletal Muscle Physiology projects are listed below. Although the majority of this work is based on widely accepted and well established animal models of muscle disorders, there is also the possibility of projects working on skeletal muscle function in humans as well.

Project 1. Factors that affect diaphragm function and contribute to breathing problems in pre-term infants. With Prof Jane Pillow, Dr Tony Bakker, Dr Peter Noble

A functional diaphragm is critically important to successful establishment of unsupported spontaneous breathing. The incidence of respiratory failure is higher in preterm babies than at any other time of life and the functional immaturity of the preterm diaphragm is likely to contribute to this respiratory failure. The preterm baby needs to generate sufficient inspiratory force to overcome the mechanical disadvantages imposed by a highly compliant chest wall, low levels of endogenous surfactant and noncompliant, structurally immature lungs. Therefore, the integrity of the diaphragm at delivery may critically influence the resilience of the infant to developing respiratory failure after birth. Optimising in utero diaphragm development and the structure and function of the diaphragm at birth is essential to ensure a healthy start to life for these extremely vulnerable babies. We aim to determine the effect of common, clinically relevant antenatal exposures (inflammation, glucocorticoids) and the timing of these insults on the metabolic, functional and structural phenotype of the fetal and newborn diaphragm.

Project 2. Unravelling the molecular processes of force enhancement in skeletal muscle.

With Dr Tony Bakker

Muscle contraction involves the cyclic interaction between myosin heads (crossbridges) on the thick filaments with binding sites on the thin (actin) filaments, a process that is driven by ATP hydrolysis. The original Huxley (1957) model for crossbridge cycling provides the foundation for current theories...
of muscle contraction and can account for various aspects of skeletal muscle function such as the force-length relationship and the force-velocity relationship during muscle shortening (concentric contraction). However, current models of muscle contraction fail to fully account for the force response when an active muscle is lengthening (eccentric contraction), or for the force enhancement observed with high frequency doublet stimulations.

Experiments on isolated muscle preparations have shown that stretch of an active muscle causes a transient increase in force arising from the strain of both contractile (crossbridges) and non-contractile (structural) components of the sarcomere. The relative contributions of these components can be determined from their force-velocity characteristics and by the use of specific myosin inhibitors (Pinniger et al., J Physiol, 2006). Structural proteins such as titin, act to stabilize the sarcomere allowing the transmission of force within and between muscle fibres and disruption to these proteins is associated with the development of exercise-induced muscle damage. Although the contribution of the structural proteins (titin) to stretch-induced force enhancement is unknown, there is evidence that titin stiffness increases upon activation in a calcium-dependent manner. This calcium dependent increase in stiffness may also account for some of the force potentiation observed with doublet stimulation.

This study aims to determine the contribution of titin filaments to calcium dependent increases in muscle stiffness. Experiments will be performed on single muscle fibres and to determine the calcium sensitivity of stretch-induced force enhancement and doublet induced force potentiation. This research is focused on unravelling the complex molecular mechanisms of tension development during muscle activation. The outcomes of this research will provide valuable insight into the mechanisms of exercise induced muscle damage and help to identify key features of the adaptation process brought about by repeated exposure to eccentric exercise.

Project 3. The role of inflammation and reactive oxygen species in skeletal muscle weakness in Duchenne Muscular Dystrophy (DMD).

With Dr Peter Arthur (Biochemistry) and Prof Miranda Grounds

Due to the absence of functional dystrophin protein, the skeletal muscles of DMD patients are inherently weaker and highly susceptible to muscle damage. Localized muscle damage and membrane lesions allow the infiltration of extracellular calcium and key inflammatory cytokines such as tumor necrosis factor (TNF) which stimulate the increased production of reactive oxygen species (ROS). The accumulation of these reactive molecules can lead to degradation of cellular constituents that can lead to cell death (myofibre necrosis). Excessive ROS production can also contribute to muscle weakness by reversible modification of protein function. We have shown that blockade of TNF activity (using cV1q, a mouse specific TNF antibody) results in a striking reduction of myofibre necrosis and muscle weakness in dystrophic mdx mice. We have also shown that anti-oxidant compounds such as N-acetyl cysteine (NAC) also reduce the severity of muscle damage and weakness in dystrophic muscle. However, our recent studies suggest that NAC may act indirectly by increasing the availability of cysteine derivatives such as taurine. This project will investigate the hypothesis that the inherent weakness in dystrophic muscle is caused by the lack of taurine availability and that taurine supplementation is a potential therapeutic treatment for DMD. Experiments will be carried out on normal healthy mice and dystrophic, mdx mice using a combination of in vivo eccentric muscle testing as well as isolated, intact muscle fibre experiments.

Suitable for: Honours, masters, PhD

Supervisor: Associate Lecturer Gavin Pinniger

Essential qualifications:
For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

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**Growing Muscles**

Myotubes (multinucleated skeletal muscle cells) are widely used as a convenient model that approximates to a muscle fibre in vivo, yet emerging data indicate that many properties of such immature cells are NOT equivalent to that of a mature, adult myofibre (discussed in Grounds & Shavlakadze, 2011). There are also be important differences between myotubes in culture and even young growing myofibres in vivo, since myofibres (both growing and mature) are innervated, in marked contrast with myotubes in culture. For example, we have shown that only GROWING muscle cells (myotubes, growing muscles and also regenerating muscles) show a signalling response to increased IGF-1. Several projects are proposed to investigate difference related to these growing and mature cells. One example is shown.

Clarifying the mechanism for impact of factors that increase (hypertrophic) or decrease (atrophic) muscles mass. Recent studies (conducted by Dr Robert White), have shown that the mechanism of action of hypertropic (IGF-1) and atrophic (TNF) factors on cultured myotubes, also involves effects on myoblast proliferation and fusion with the growing myotube: this is in addition to effects on signalling pathways related to protein synthesis and degradation that result in net protein content (paper in progress). A new project will examine the effects of 2 forms of Vitamin D on these models of cultured C2C12 myogenic cells, primary cultures of muscles cells and isolated myofibres.

Non-coding RNA expression during the different phases of post-natal muscle growth Other studies in our group by PhD student Ms Laurent Butchart have profiled the expression patterns of many RNAs (mRNAs, miRNAs and long non-coding RNAs) throughout the post-natal growth of normal mouse muscles (paper under review). New projects can extend this approach to studies of muscular dystrophies.


1. Isolated Myofibres as a model for growth factor responses
2. Investigating sarcolemma properties of growing and adult myofibres: imaging studies and mechanobiology
3. The mystery of central myonuclei in regenerated mouse muscles
Aging Muscles

Skeletal muscles constitute approximately 40% of the mass of the human body and are essential for all aspects of movement such as breathing, eating, posture, walking and reflexes as well as heat generation and metabolism. A loss of muscle mass, known as atrophy or wasting, has major consequences for strength and muscle function. Muscle wasting can result from disuse (e.g. bed rest or space travel), injury, starvation, diseases such as cancer, sepsis, neuromuscular disorders, and also ageing. Different factors contribute to muscle wasting in the various conditions. The progressive loss of muscle mass associated with ageing is known as sarcopenia and is the focus of this research. Between the ages of 50 and 80 years in humans, muscle mass is reduced by about one-third; this is a major contributing factor to increased falls and fractures, with impaired physical function (frailty) resulting in dependency and sometimes death. Development of new targeted interventions to reduce sarcopenia and frailty would have a major impact on reducing health system costs, as well as improving the quality of life for the growing population of older individuals. In order to develop appropriate interventions to reduce muscle-wasting we need to understand the key factors responsible for sarcopenia. This is the focus of our current research.

Our research includes student projects on muscles and also the nervous system related to the role of denervation in sarcopenia; the role of protein degradation in sarcopenia, analyses of mitochondrial function and/or epigenetics in sarcopenia; molecular analyses and biomarkers of ageing in mice and humans.


See also recent papers 2010- 2013 on http://school.anhb.uwa.edu.au/personalpages/grounds/

Project is suitable for Honours, PhD

Chief supervisor Prof. Miranda Grounds

Other supervisors Prof. Alan Harvey. Ms Zoe Soffe, Ms Vidya Nambiar (PhD students),
Dystrophic Muscles

A major focus of our research is developing therapies for muscular dystrophies, using the mdx mouse (e.g Project 1 below). More recently we have been investigating dysferlinopathies using dysferlin-deficient A/J and BLAJ mice (Project 2). This research is of central interest to various parent and other international groups. e.g TreatNMD http://www.treat-nmd.eu/

Project 1. Potential drug treatment for DMD. The aim is optimise the use of taurine to reduce disease severity on the mdx mouse model. We have much experience in this area and the research is funded by an NHMRC grant.


This project would be done in close collaborations with Dr Jessica Terrill and Dr Peter Arthur (UWA) who are experts on these studies on dystrophic mdx mice and all associated biochemical analyses, often related to oxidative stress.

Project 2. Lipids and dysferlinopathies. The aim is to define the MECHANISM for the high lipid content and expansion of adipocyte populations in dysferlin-deficient muscles. This is based on novel observations made in our laboratory regarding the reasons for disease in dysferlin-deficient muscles.


Tissue culture and mouse experiments are in progress to pursue this new research and these are evolving and can be discussed.

Project is suitable for Honours, PhD

Chief supervisor Prof Miranda Grounds

Other supervisors Dr Peter Arthur, Dr Jessica Terrill, Dr Robert White

Essential qualifications

For Honours: An appropriate undergraduate degree with a biological science emphasis, and a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree with a biological science emphasis or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.
Sleep Science – Sleep and its Disorders

Obstructive sleep apnoea is a common condition, affecting as many as 2-4% of middle-aged adults, and is accompanied by heavy snoring. It is characterised by repetitive partial or complete collapse of the upper airway (throat) during sleep. These episodes, which can occur hundreds of times during a single night, are accompanied by a momentary fall in blood oxygen levels, an increase in blood pressure and arousal. These disruptions result in excessive daytime tiredness and lethargy.

Sleep researchers at the School of Anatomy, Physiology & Human Biology (UWA) and the West Australian Sleep Disorders Research Institute (Sir Charles Gairdner Hospital) have an active interest in understanding factors that predispose individuals to obstructive sleep apnoea. Large numbers of patients are seen at the hospital clinic each year, most of whom are suitable for participation in research studies. Hospital-based projects are available in waking and/or sleeping individuals with and without sleep disorders.

A major NHMRC-funded project has recently been completed at the School’s Centre for Sleep Science, located on the UWA campus near the School of Anatomy, Physiology & Human Biology. The study has funded full overnight sleep studies on 1,000 healthy 23 years olds who are participants in the WA Raine Study Cohort. The purpose of the study is to determine the prevalence of sleep disorders in young adults, and investigate the factors that lead to sleep disorders in this age group. The extensive, unique data being collected as part of this study is also available for research projects. Competitive Raine Foundation PhD scholarship top-up awards are available.

Other active areas of research in which projects are potentially available include: stroke and sleep disorders; gastroesophageal reflux and sleep disorders; craniofacial structure and sleep disorders; sleep and neurocognitive function; sleep and athletic performance; and cardiovascular function and sleep disorders.

Project is suitable for: Honours, Masters, PhD

Supervisor: Prof Peter Eastwood

Other supervisors: Dr Jennifer Walsh, UWA and Sir Charles Gairdner Hospital
Dr Kelly Shepherd, UWA and Sir Charles Gairdner Hospital
Clinical Professor David Hillman, Sir Charles Gairdner Hospital
Dr Nigel McArdle, Sir Charles Gairdner Hospital

Essential qualifications

For Honours: An appropriate undergraduate degree with a biological science emphasis, and a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree with a biological science emphasis or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.
**Stem Cell Mechanobiology**

My research focus is in controlling stem cell fate by providing different microenvironments. The fate of stem cells were thought to be primarily dictated by biochemical signals including cytokines and growth factors for decades, however, more recent data suggested stem cells also responded to their neighbouring cells and extracellular matrices (ECMs). Previously, I have shown that stem cells from fat (adipose-derived stem cells – ASCs) were able to feel/sense and respond (mechansense) to matrices mimicked stiffness of brain, skeletal muscle, and bone and committed to differentiate into those tissue lineages, respectively. Intracellularly, stem cells transduce these biophysical/mechanical signals into biochemical signals from cell membrane to nucleus and this process is called mechanotransduction. Our group aims to study how mechanical cues (especially stiffness) control stem cells by focusing on 3 areas: 1) investigating intracellular mechanism how stem cells respond to ECM mechanical cues, 2) developing bio-inspired ECM (2D and 3D biomaterials) as platforms to control stem cell fate, 3) programming stem cells to be used in stem cell therapy, tissue engineering and regenerative medicine.

**Project 1. Mechanosensing-driven stem cell differentiation on high-throughput stiffness gradient hydrogel with micropatterns**

*With Associate Professor Adam Engler at University of California, San Diego (UCSD)*

Adipose-derived stem cells (ASC) which could be isolated from patient by minimal invasive procedure, liposuction, has known to be capable of rapid growth (regenerating large volume of tissue) and skeletal muscle or fat differentiation. Previously, osteogenic (bone) and adipogenic (fat) differentiation has been heavily relied on biochemical methods, however, the efficiency remains questionable for large volume regeneration. More recently, it has been shown that surrounding extracellular matrix (ECM) could also influence the fate of stem cells. Particularly in respect to stiffness (one of the mechanical properties of ECM), my previous studies showed that ASCs were able to ‘feel’ and/or ‘sense’ how stiff the underneath was when cultured on hydrogels that mimicked stiffness of bone or adipose tissues without biochemical induction and be differentiated into bone or fat cells, respectively. Others also showed that ECM protein composition played significant role in stem cell differentiation as well as geometry, which will decide cell shape and size. Their combinatorial (biochemical and biomechanical) induction has yet to be examined. The aim of this project is to develop a high-throughput screening platform to examine the most synergistic combinations of biochemical and biomechanical induction for bone or fat cell differentiation. For high-throughput screening, stiffness gradient hydrogel (stiffness ranges from fat-like soft to bone-like hard) was fabricated using two-layer hydrogel polymerization technique. Micro-contact printing technique will be used to stamp different ECM proteins (e.g. collagen) with different shapes and sizes on the stiffness gradient gel to test best combination of stiffness, ECM protein composition and shape/size. To summarize, this platform will allow us to test stem cell differentiation with 6 stiffness, 6 ECM proteins, 6 shape/size, and 6 biochemical induction media by 6 repeats in one 6-well plate. This high-throughput screening platform will ‘speed up’ tissue engineering approach using stem cells to regenerate bone and fat tissues.

**Project 2. Role of YAP/TAZ in stem cell mechanotransduction, differentiation, and migration**

*With Prof. Kun-Liang Guan and Dr. Henry Park at UCSD*

There are several pathways and key signaling molecules suggested in mechanotransduction. Most of suggested pathways involve focal adhesion with extracellular binding of integrin to ECM protein as a starting point and intracellular interaction of beta unit of integrin to actin-myosin through focal
adhesion kinase (FAK), talin, and vinculin binding. Intracellular forces generated by different matrix stiffness will decide localization (cytoplasmic vs. nucleic) of YAP/TAZ (transcriptional coactivator in Hippo pathway), which will control transcriptional level as a final step. Bone marrow-derived stem cells exhibited cytoplasmic localization of YAP/TAZ on soft hydrogel (fat-like stiffness) but YAP/TAZ was localized in nuclei on stiffer hydrogel (bone-like stiffness). Differentiations into fat and bone lineages were also observed and YAP/TAZ overexpression or knockdown cells altered mechanical induction (no bone differentiation on bone-like stiffness when YAP/TAZ knock-downed). Most studies with YAP/TAZ assumed it as a downstream of mechanosensing but more recent results (YAP/TAZ changes integrin expression profile in cancer research) suggest that YAP/TAZ may have feedback effect to ‘feeling’ or YAP/TAZ act as upstream of ‘feeling’ as well. In this project, we aim to investigate the effect of YAP/TAZ on mechanosensing (once considered as upstream of YAP/TAZ) in the context of intracellular force generation (direct response from extracellular stiffness), migration, and differentiation.

Project 3. Mechanotransduction driven cardiac differentiation of stem cells
This project focuses on generating novel targeted therapies for triple negative breast cancers. Triple negative breast cancers are responsible for most of the deaths related to breast cancer in Australia and in the world. These cancers do not express oestrogen receptor alpha, progesterone receptor and epidermal growth factor receptor 2, targets typically exploited in the clinic. They belong to the basal-like subtype breast cancer, comprising 15% of all breast cancers. In the metastatic setting they are highly resistant to chemotherapy. DNA-damaging agents used in chemotherapy, lacking target selectivity have generalized side effects. Thus, there is an urgent need to develop novel, more specific and targeted molecular approaches to treat this lethal disease.

Project 4. N-cadherin-mediated cell-cell and integrin-mediated cell-ECM mechanotransduction in heart
The human heart, a mechanically dynamic tissue, pumps out ~5L of blood/ minute. At tissue level, its mechanical function has been widely studied, but little is known at cellular level how cardiac muscle cells mechanically coordinate their beating with neighboring cells or how mechanical extracellular stimuli dictate cardiac muscle cell behavior. One cardiac muscle cell in vivo may make three principal connections with its surroundings (i) cell-ECM adhesion via integrin-mediated focal adhesion, (ii) cell-cell adhesion via N-cadherin, and (iii) cell-cell gap junction with ion channels including the calcium channel. In disease models in particular, not only biochemical signaling changes but also the mechanical environment alters the cell’s behavior via these 3 main connections. For example after myocardial infarction (MI), excessive deposition of collagen causes greater ECM stiffness, which may alter focal adhesion complex / actinin (i.e. the Z-band – an important structure bearing contractile forces) and disrupt cytoskeletal structure resulting in loss of contraction and alteration of cell-cell interaction via N-cadherin. This project aims to address how these 3 main connections (N-cadherin, focal adhesion, and gap junction) control the cardiomyocyte’s function in disease. Three specific aims address 1) the effects of ECM stiffness on cardiomyocyte function; cell-ECM mechanotransduction, 2) mechanosensitivity of cardiomyocyte via N-cadherin; cell-cell mechanotransduction, and 3) ion handling capacity, especially calcium which is the main driving force for cardiomyocyte contraction, examining different cell-cell / cell-ECM situations

Project 5. Stem cell mechanotransduction in osteochondral tissue engineering
The causes associated with osteochondral defects vary from natural wearing to trauma related injuries. With ageing, the natural degradation or wearing of the cartilage often leads to osteoarthritis. Tissue engineering approaches have emerged in last two decades to regenerate damaged tissues using biomaterials, stem cells, and supplementary biochemical. One of the challenges in osteochondral tissue engineering was to fabricate or mimic bilayer structures at the
border of articular cartilage and bone, which can further divided into superficial zone, middle zone, deep zone/calcified cartilage, and subchondral bone. As ECM components per zone from cartilage to bone vary, their compressive modulus (stiffness) show huge ranges in order of magnitude from 79KPa, 2.1MPa, 320MPa, and 5.7GPa where cells mechanosense very differently. Here, we aim to develop biomaterials that mimic stiffness step gradient to examine how stem cell mechanotransduction plays role in osteochondral tissue engineering. Stiffness step gradient hydrogel will be fabricated using two-layer hydrogel polymerization technique modified from my previous research. Bone marrow-derived stem cells and adipose-derived stem cells will be tested their chondro- and osteo-genic capacity on biomaterials and their mechanotransduction will also be studied. Once this reductionist approach provide answers in mechanosensing of stem cells per stiffness, biochemical component of ECM can be added up to investigate synergistical effect of biomechanical (stiffness) and biochemical (ECM components) in osteochondral tissue engineering. To summarize, this study will enhance our understanding in mechanical influence at cellular level in both chondro- and osteo-genic regeneration and also provide deep insight for biomaterials fabrication in osteochondral tissue engineering.

Project is suitable for Honours, Masters, PhD
Supervisor: Dr Yu Suk Choi

Essential qualifications
For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.