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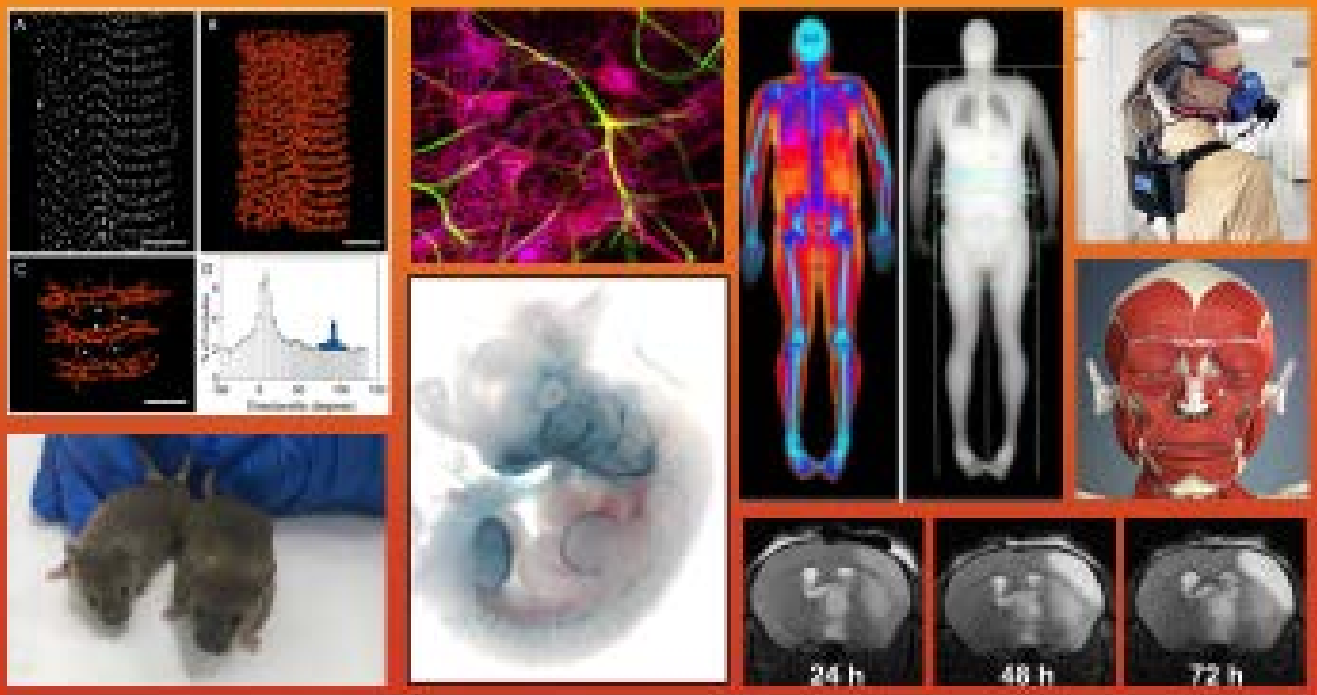
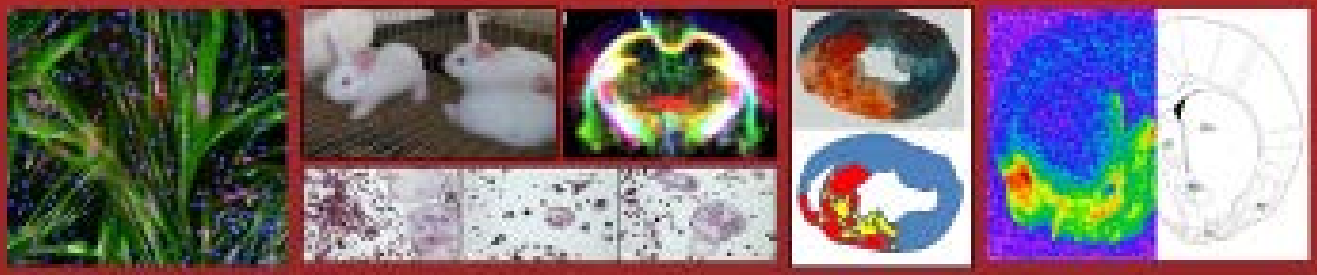


Department of Physiology, Anatomy and Microbiology

Honours in Physiology & Anatomy (HBS4HPA)



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Potential Honours projects in HBS4HPA 2020

Below is a list of projects that are being offered by the Department of PAM in 2020. Please note that not all of these projects will be based at the Bundoora campus and some may require working at other locations (e.g. the Baker Institute) – it would be a good idea to discuss logistics with any potential supervisor before applying for a particular project. Please remember: **You will NOT be offered a project by a supervisor if you haven't met with them**. Make sure you get in contact with the supervisors of any projects that interest you and discuss their (and your) expectations of what the successful applicant would be doing next year. Please also note: this is not a definitive list of all projects and it is highly likely that more projects will be added to this list towards the end of the year.

If you have any questions about the projects or how the Honours year works, don't hesitate to contact potential supervisors or myself (j.church@latrobe.edu.au).

Regards,

Jarrod Church (Hons coordinator)

Project #1: The search for genes involved in craniofacial development

Supervisor(s): Dr. Seb Dworkin and A/Prof. Brian Grills

Background: Genetic mutations during embryonic development can lead to lifelong debilitating effects on health, social wellbeing and physical development. Mutations which affect the skull, face palate and lower jaw are present in approximately 1:1,000 births, and necessitate in extensive and expensive surgery, hospitalisation and ongoing treatment. Understanding the identity and function of genes which play a role in normal cranio-facial development is therefore important in identifying genetic and biochemical pathways which may be targets for pre-natal treatment, thereby lessening the severity of cranio-facial defects at birth. Using the well-characterised zebrafish model at La Trobe University's brand new Aquatic Research Facility, this project will identify novel genes which contribute to the formation and development of the bones which comprise the face, palate and skull.

Aims: This project will involve the generation and characterisation of novel zebrafish mutant lines using the cutting edge technique of CRISPR/Cas9-mediated deletion.

Key Scientific Skills: The student will receive training in zebrafish husbandry and breeding, oocyte microinjection, computer (in silico) analysis of genomic datasets, PCR and in-situ hybridisation.

Further information: If you are interested in learning more about this project please contact Seb Dworkin (s.dworkin@latrobe.edu.au).

Project #2: Using Amnion Cells to Treat Ischemic Stroke

Supervisors: Prof. Chris Sobey, Dr. Richard Zhang

Background: Stroke is the leading cause of death and disability worldwide. It is associated with either an interruption of brain blood flow caused by the blockage of a cerebral artery by a blood clot (ischemic stroke) or bleeding from a cerebral blood vessel (hemorrhagic stroke). Currently the only treatment available for ischemic stroke is the use of a clot-buster drug (i.e. a thrombolytic) to dissolve blood clot within 4.5 h of onset. Our recent experimental work has established intravenous administration of human amnion epithelial cells (hAECs) to be a powerful treatment to reduce brain injury and inflammation as well as neurological deficits. As a result of our recent experimental work, a clinical trial has commenced to test hAECs in human stroke patients. The next phases of our experimental work will continue in mouse models of stroke to assess the effectiveness of hAECs in combination with a thrombolytic agent in ischemic stroke. Although it is understood that thrombolytics may promote bleeding in the brain following stroke (i.e. hemorrhagic transformation), we do not know whether hAECs might exert protection against this effect.

Aim: These projects will investigate the therapeutic effect of hAECs in combination with a thrombolyitic following middle cerebral artery occlusion in mice. In addition, mice with subarachnoid hemorrhage will be studied to assess the effects of hAECs on recovery from brain hemorrhage.

Key Scientific Skills: Students will receive training in advanced laboratory research skills including animal handling, behavioural deficit assessment on mice following stroke, as well as expertise in histology, brain infarct analyses, immune cell infiltration and inflammatory markers in brain tissue following stroke.

Further information: If you are interested in learning more about this project, contact Prof. Chris Sobey c.sobey@latrobe.edu.au or Dr. Richard Zhang s.zhang@latrobe.edu.au

Project #3: Obesity in pregnancy and the effect of intermittent fasting

Supervisors: Dr Maria Jelinic and Dr Tania Romano Stasis

Background: Over 50% of Australian women are overweight or obese including 35% of women aged 25-35 years of age. As a result of increased obesity in these reproductive years, the prevalence of obesity in pregnancy is also rising. Obesity in pregnancy increases complications of labour and delivery and also has deleterious effects on fetal programming, predisposing offspring to adverse cardiometabolic and neurodevelopmental outcomes. Intermittent fasting is an effective and natural strategy for weight control, but the effects of its use in pregnancy is poorly understood. Recent preliminary studies indicate that Ramadan fasting in pregnant women had positive maternal outcomes (lowered abdominal visceral fat mass and rate of gestational diabetes). However, the effects of fasting on fetal outcomes are poorly defined. Using a diet-induced mouse model of obesity, this honours project aims to test the effects of the 16:8 fasting diet in mid-pregnancy on maternal and fetal outcomes. Female mice will be fed a high fat diet for a minimum of 6 weeks prior to mating. Non-obese control mice maintained on a normal chow diet will be studied in parallel. On day 11 of pregnancy (the mouse equivalent of the human 2nd trimester), mice will begin intermittent fasting (16 hours, with the 8 non-fasting hours during the active phase and mice are able to eat ad libitum). Several *in vivo* physiological parameters will be measured at various timepoints throughout the study (baseline, pre-mating, day 10 and day 17) including: body weight; food and water intake; blood glucose; renal function including albuminuria and creatinine clearance; blood pressure (tail-cuff and radiotelemetry); and renal artery

blood flow and stiffness (high resolution ultrasound imaging). On day 18 of pregnancy major organs (kidneys, heart, aorta, liver, placentae etc) and fetal measurements will be collected to examine the cellular composition and pro-inflammatory cytokine/adipokine profiles using qPCR, flow cytometry and immunohistochemistry.

Aims: To determine the cardiorenal and fetal outcomes following intermittent fasting in obese and non-obese pregnancy.

Key Scientific Skills: The student will receive training in mouse handling (incl. blood collections, non-invasive tail cuff blood pressure analysis), qPCR analysis, flow cytometry, and histopathology/ immunohistochemistry.

Further information: If you are interested in learning more about this project please contact either Maria Jelinic (m.jelinic@latrobe.edu.au) or Tania Romano Stasis (t.romano@latrobe.edu.au).

Project #4: Single-Cell Transcriptional Profiling of the Hypertensive Mouse Aorta and Kidney.

Supervisors: Dr Antony (Bill) Vinh, Dr Maria Jelinic, Dr Alexander Pinto and Prof Grant Drummond

Background: High blood pressure, also known as hypertension, remains the leading risk factor for cardiovascular diseases. Surprisingly, the cause of ~90% of clinical cases of hypertension remains unknown, and as a result, current anti-hypertensive therapies mainly target symptoms of high BP, rather than the cause. Recently, inflammation and immunity have been implicated in the development of hypertension. It is hypothesised that activation of the immune system during hypertension, promotes local inflammation in vital blood pressure controlling organs including blood vessels and the kidney, which is characterised by excessive accumulation of immune cells including T cells and macrophages. While we and others have reported that hypertension is strongly associated with elevated infiltration of immune cells into aorta and kidney of hypertension mouse models, the precise mechanisms by which they promote vascular and renal dysfunction remain unclear. Using state-of-the-art *single cell RNA sequencing (scRNA-seq)*, combined with cutting-edge bioinformatics, this honours project aims to define the vascular and renal cellular networks, as well as the genetic and paracrine signalling pathways that are involved in hypertension. This project will use *multiparameter flow cytometry* to define the cellular heterogeneity of the aortae and kidneys from hypertensive mice compared to normotensive controls. Using scRNA-seq, this project will examine gene expression at the single cell level which will involve creating RNA libraries to form clusters of genes that identify with each cell of the aorta and kidneys. From these libraries, we will be able to determine the relative gene expression for each cell that are differentially expressed in aorta and kidneys from hypertension mice compared to normotensive controls. The major outcome of this project is to identify novel pathways in the context of hypertension, which might be exploited as biomarkers of disease severity or as targets for new anti-hypertensive therapies

Aims: To determine the cellular and paracrine signalling events that ultimately give rise to vascular and renal inflammation during hypertension

Key Scientific Skills: Students will gain experience in mouse procedures including the surgical induction of hypertension and tail cuff blood pressure measurements. Other techniques include multiparameter flow cytometry, immunohistochemistry and complex bioinformatic analyses of scRNA-seq data.

Further information: If you are interested in learning more about this project please contact either Bill Vinh (a.vinh@latrobe.edu.au), Maria Jelinic (m.jelinic@latrobe.edu.au) or Grant Drummond (g.drummond@latrobe.edu.au).

Project #5: The role of the IL-18/IL-18R signalling axis on vascular remodelling in a mouse model of abdominal aortic aneurysms

Supervisor(s): Dr Antony (Bill) Vinh, Dr Quynh Dinh and Prof Grant Drummond

Background: Abdominal aortic aneurysms (AAA) affect approximately 13% of the adult population aged over 65, and ruptured aneurysms can lead to internal bleeding, which is often fatal. There are currently no pharmacological approaches to prevent or control AAA expansion, with surgical intervention as the only option, which always includes a degree of risk. While the pathogenesis of AAA formation remains unclear, inflammation has recently been implicated in the remodelling of blood vessels leading to expansion and eventual rupture. An important inflammatory pathway involved in innate immunity is the inflammasome, which functions to release pro-inflammatory cytokines in response to various pathogen and stimuli. Interleukin (IL)-18 is an inflammasome-derived cytokine that binds to its cognate IL-18R receptor to induce promote local inflammation. We have striking new data that IL-18-knockout mice are completed protected (IL-18KO: 0% vs WT: 57%) against AAA formation in the angiotensin II-model of AAA. In contrast, the IL-18R-knockout mice showed significantly greater incidence of AAA formation compared to wildtype (WT) mice using a mild model of AAA formation (IL-18RKO: 86% vs WT: 57%). Collectively, this data suggests that while IL-18 appears to promote AAA, an alternative pathway that acts on the IL-18R may actually protect against AAA formation. We now aim to further examine the mechanisms associated with the greater incidence in the IL-18R-KO mice. This project will characterise the vascular structure and expression of extracellular matrix-degrading enzymes in IL-18R-KO mice compared to WT mice. Secondly, using a new strain of mice (IL-18R accessory protein KO) that genetically ablates the IL-18 signalling pathway specifically, but preserves the function of IL-18R, we aim to delineate the IL-18R-mediated protective mechanisms that may be associated with AAA formation. By understanding the role of IL-18R in the formation of AAAs, we may identify novel therapeutic targets to pharmacologically control AAA progression and/or rupture.

Aims: To define the role of IL-18R on vascular remodelling and AAA formation

Key Scientific Skills: Students will have experience with procedures mice including the induction of hypertension and *in vivo* ultrasound of mouse abdominal aorta. Other techniques include tail cuff blood pressure measurements, RT-PCR, flow cytometry, immunohistochemistry and histology.

Further information: If you are interested in learning more about this project please contact either Bill Vinh (a.vinh @latrobe.edu.au) or Quynh Dinh (q.dinh@latrobe.edu.au).

Project #6: Is a 'fat heart' an especially vulnerable heart?

Supervisor(s): Dr. Jim Bell

Background: Maintaining normal rhythm properties is essential to heart function. Sustained arrhythmias (including atrial fibrillation) increase significantly with aging and in obesity. Often evident in otherwise 'healthy' asymptomatic patients, these sustained arrhythmias represent a primary component of cardiac demise. Understanding the cellular mechanisms driving arrhythmias is crucial to developing new effective therapies. Recent evidence has emerged indicating that accumulation of the fat around the heart (pericardial adipose) may be crucial to the development of sustained arrhythmias in the aged/obese population. Pericardial adipose levels are known to increase markedly in obesity, with aging, and in post-menopausal women – all important risk factors for cardiovascular disease. Our very recent data indicate that pericardial

adipose may release proteins that exert a paracrine effect on the heart muscle to increase vulnerability to arrhythmias. This project will use molecular and tissue recording studies of human and rodent tissues to further understand how cardiac adipose contributes to the development of cardiac arrhythmias.

Aims: This project will use molecular and tissue recording studies of rodent tissues to further understand how cardiac adipose contributes to the development of cardiac arrhythmias.

Key Scientific Skills: The student will receive training in rodent colony maintenance, isolated heart perfusion & electromechanical performance assessment, protein biochemistry and histology.

Further information: If you are interested in learning more about this project please contact Jim Bell (j.bell@latrobe.edu.au)

Project #7: Understanding the role of locally synthesised steroids in the heart

Supervisor(s): Dr. Jim Bell

Background: Important differences exist between women and men with regard to cardiovascular disease. This is likely related to sex steroid (estrogen and testosterone) actions on the heart. However, recent controversies about the use of sex steroid therapies in men and women highlight a lack of understanding of the underlying mechanisms by which sex and sex steroids influence the heart. We have recently shown in humans that both the myocardium and cardiac adipose express the enzyme aromatase – showing that estrogen synthesis can actually occur within the myocardium. In aging/obesity, when the onset of cardiovascular disease is prominent, the influence of this locally-synthesised estrogen likely increases.

Aims: This project will use molecular and tissue recording studies of rodent tissues to determine how estrogens synthesised within the heart contribute to the development of cardiac rhythm and relaxation abnormalities.

Key Scientific Skills: The student will receive training in rodent colony maintenance, isolated heart perfusion & electromechanical performance assessment, protein biochemistry and histology.

Further information: If you are interested in learning more about this project please contact Jim Bell (j.bell@latrobe.edu.au)

Project #8: Role of estrogen signalling in post-stroke cognitive function

Supervisor(s): Dr. Quynh Nhu Dinh, Prof. Chris Sobey

Background: Stroke is a leading cause of death and disability worldwide. Cognitive impairment commonly occurs after a stroke with ~30% of stroke patients developing dementia. Pre-clinical data have suggested that estrogen has a neuroprotective role during stroke and our laboratory has reported that targeting the estrogen receptor, GPER, can influence stroke outcome in a sex-dependent manner. Furthermore, while activation of GPER has been reported to improve cognitive function after traumatic brain injury, the contribution of GPER to post-stroke cognitive function is not yet known.

Aims: This project aims to determine whether deletion of GPER will impact normal memory function and specifically worsen post-stroke cognitive function. This project will utilize male and female GPER-deficient mice that have been developed by our laboratory.

Key Scientific Skills: The student will receive training in many advanced laboratory research skills including stroke surgeries, laser speckle contrast imaging to measure cerebral blood flow, cognitive testing and histology.

Further information: If you are interested in learning more about this project please contact Quynh (q.dinh@latrobe.edu.au) or Chris (c.sobey@latrobe.edu.au).

Project #9: Can Nicotinamide Mononuceotide (NMN) improve muscle function and reduce muscle fatigue?

Supervisors: Dr Chris van der Poel, Dr Caroline Taylor and Dr Jarrod Church

Background: Exercise can result in up to a 1,000-fold increase in the rate of ATP demand compared to that at rest. However skeletal muscle stores a relatively small amount of ATP and as such relies on other mechanisms to generate ATP to sustain prolonged activity. Skeletal muscle cells can contain thousands of mitochondria, which require sufficient levels of nicotinamide adenine dinucleotide (NAD+) to drive the aerobic/oxidative production of ATP. Levels of NAD+ have been shown to be important in several processes including mitochondrial biogenesis, gene transcription, and organization of the muscle extracellular matrix. Recent studies have suggested that low levels of NAD+ are deleterious for muscle health and higher NAD+ levels augment muscle health.

Aims: This project will supplement mice with a NAD+ intermediate, nicotinamide mononuceotide (NMN), to investigate whether increasing levels of NAD+ in healthy mice improves muscle function and reduces muscle fatigue.

Key Scientific Skills: This project will involve animal handling, animal injections, animal surgery, biochemistry and histology

Further information: If you are interested in learning more about this project please contact Chris (C.VanDerPoel@latrobe.edu.au).

Project #10: Modulation of brain astrocytes to improve neuronal survival

Supervisor(s): Dr. Ross O'Shea and Dr Michael De Silva

Background: Neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Huntington's disease and Motor Neurone Disease are becoming increasingly prevalent with the increasing life expectancy of our population. These diseases result from the death of specific populations of neurones in the central nervous system; the symptoms of individual diseases reflect the loss of function normally associated with those neurones. Neurodegenerative diseases are chronic and fatal, and current therapies are only able to treat the symptoms without slowing disease progression.

Astrocytes are the most abundant population of non-neuronal cells of the central nervous system. These cells are extremely plastic and normally perform vital roles that maintain neuronal survival. The activity of

astrocytes is commonly impaired in neurodegenerative diseases; although these cells generally survive, their ability to promote neuronal viability is impaired. There is also evidence showing that astrocytes can actually initiate neuronal death in these diseases).

Numerous in vitro studies have demonstrated that astrocytes can be modulated in order to stimulate activities that support neuronal survival, and our previous work has identified Rho-associated Kinases (ROCK1 and ROCK2) as an important regulators of astrocytic structure and function.

Aims: This project aims to investigate whether antisense RNA selectively inhibiting either ROCK1 or ROCK2 has differential effects on astrocytes that might promote neuronal survival.

Key Scientific Skills: The student will receive training in cell culture, cell viability assays, immunohistochemistry, biochemical assays and Western Blotting.

Further information: If you are interested in learning more about this project please contact Ross O'Shea (r.oshea@latrobe.edu.au)

Project #11: Elucidating the protective role of interleukin-37 in kidney disease

Supervisor(s): Dr Brooke Huuskes, Dr Antony (Bill) Vinh

Background: There are many factors that can cause kidney failure. Regardless of the initial cause, inflammation in the kidney is always present and drives the progression of chronic kidney disease to end-stage kidney disease. Kidney inflammation is perpetuated though cells of the immune system infiltrating into the kidney and releasing pro-inflammatory cytokines, causing further inflammation. Interleukin (IL)-18 is one such cytokine and signals T cells. Recently a regulator inflammation has been discovered, interleukin (IL)-37. IL-37 can signal to cause the release of anti-inflammatory cytokines in addition to preventing the pro-inflammatory downstream signalling of IL-18. The role of IL-37 and its ability to prevent kidney inflammation has not yet been explored. This is an exciting opportunity to determine the contribution of IL-37 in kidney disease and understand the mechanism of IL-37 signalling. By understanding these processes we can possibly identify new targets for therapies which will help lessen the burden of kidney disease.

Aims: This project aims to characterise the IL-37 signalling pathway in mouse models of kidney disease.

Key Scientific Skills: Students will have experience with animal surgical techniques including the induction of hypertension, hypoxia and fibrosis. Other techniques will involve taking blood pressure readings, PCR, flow cytometry, kidney histology and single cell RNA sequencing

Further information: If you are interested in learning more about this project please contact either Brooke (b.huuskes@latrobe.edu.au) or Bill (a.vinh @latrobe.edu.au)

Project #12: Role of endothelial PPARγ in ischemic stroke

Supervisor(s): Dr Michael De Silva and Prof Chris Sobey

Background: Stroke is a major cause of death and disability worldwide. The endothelium (inner lining of blood vessels) plays an important role in maintaining vascular homeostasis including supressing thrombosis, inflammation and regulating artery diameter. Importantly, dysfunction of the endothelium is a key initiating event in many cardiovascular diseases. The transcription factor peroxisome proliferator-activated receptor γ (PPARγ) serves as a major endogenous protective molecule in the vasculature. However, the contribution of endothelial PPARγ to stroke outcome is unknown.

Aims: This project will test whether endothelial PPARγ can protect the brain and the cerebral vasculature against ischemic stroke damage. To test this, we will use mice that overexpress either active or dysfunctional PPARγ only in endothelial cells.

Key Scientific Skills: The student will receive training in surgical procedures, assessing behavioural deficits, brain infarct size, blood vessel function, gene expression, immune cell infiltration and inflammatory markers in mice following stroke.

Further information: If you are interested in learning more about this project please contact Michael (t.desilva@latrobe.edu.au).

Project #13: High blood pressure and dementia: a role for the immune system

Supervisor(s): Dr Michael De Silva, Dr Antony Vinh and Prof Chris Sobey

Background: Vascular dementia is defined as cognitive imapiairment as a result of cerebrovascular pathologies and is the second most common form of dementia behind Alzheimer's disease. Hypertension is a major risk factor for cerebral artery dysfunction and disease, including vascular dementia. There is strong evidence linking hypertension with inflammation and accumulation of immune cells such as T cells and macrophages in the vasculature. We have developed novel techniques to measure accumulation of these cells within large conduit and resistance vessels. However, an in depth analyses of immune cell infiltration into the cerebral vasculature remains understudied.

Aims: This project aims to correlate cerebrovascular inflammation with the development of hypertension and cognitive impairment. We will also examine the effect of pharmacological immunosuppression on cognitive function in the setting of hypertension. The outcomes of this study will provide experimental evidence that inflammation may be a link between hypertension and cognitive impairment.

Key Scientific Skills: The student will receive training in minor surgical procedures (mini-pump implantations, tail vein injections) and *in vivo* blood pressure monitoring (tail cuff plethysmography) in mice, brain blood flow measurements (laser speckle contrast imaging), immunological (flow cytometry) and confocal imaging techniques on isolated tissues to assess inflammation. Moreover, this study will correlate changes in blood pressure and inflammation with cognitive function measured by state of the art behavioural testing.

Further information: If you are interested in learning more about this project please contact Michael (t.desilva@latrobe.edu.au).

Project #14: Anatomy Virtual and Augmented Reality systems: Effect of Immersive Technologies on Student Engagement and Outcomes

Supervisors: Heath McGowan, Dr Aaron McDonald

Background: This project will evaluate the effect of 'Augmented Reality (AR)' and 'Virtual Reality (VR)' on students' and staff's experiences, and student outcomes and engagement in a second-year anatomy subject at La Trobe University (HBS2HAA). There will also be scope to investigate further digital technologies and funding opportunities.

Anatomy is a foundation discipline delivered to approximately 4,300 students in a given year. The Anatomy Discipline propose to adopt Virtual and Augmented Reality in its teaching in a move towards "digital anatomy". AR & VR have been shown to be more engaging and interactive than 3D models, and shown to increase learning outcomes and improve knowledge retention and spatial ability in this highly visual field of study. This technology will be implemented in an increasing number of subjects and evaluated to inform the role AR and VR should take in our teaching. This program will then expand throughout 5 campuses.

Aims: Specific aims of the study are:

1. To evaluate the effect of AR & VR technologies on students' learning experience.
2. To quantify the effect of AR & VR technologies on student engagement (contribution to LMS discussion forums) and outcomes (in-semester assessment and final exam marks).
3. To evaluate the experience of demonstrators' teaching using immersive digital technologies.

Key Scientific Skills: The student will gain experience in both qualitative and quantitative research techniques and different analysis methods, including statistical analysis of quantitative data and thematic analysis of qualitative data.

Further information: If you are interested in learning more about this project please contact either Heath (H.McGowan@latrobe.edu.au) or Aaron (A.McDonald@latrobe.edu.au).

Project #15: Evaluation of an employability program embedded into the non-vocational Bachelor of Health Sciences course.

Supervisors: Dr Louise Lexis, Dr Brianna Julien, Professor Birgit Loch

Background: Although it is clear that the higher education sector places a high value on graduate employability, research and practice in this area are under-developed. La Trobe University's Bachelor of Health Sciences is a non- vocational 3-year course with over 1000 students and is the stepping-stone to at least 30 identified career pathways. The course previously had a sparse and piecemeal approach to the development of students' employability skills which were largely confined to the third and final year. To remedy this, a collaborative project involving Health Sciences and Careers and Employability staff is underway to introduce a scaffolded course-wide curriculum which will be integrated into targeted core subjects at each level and semester of the course. The curriculum is underpinned by La Trobe University's recently introduced Career Ready Capability Framework and Career Ready Advantage program and drawing on the connectedness pedagogies presented in the Graduate Employability 2.0 Connectedness Learning Model. The curriculum is intended to enable students to graduate with (1) a functioning professional social network and the ability to

form and maintain professional relationships, (2) digital career literacy, and (3) the ability to apply their connectedness and Career Ready capabilities in the innovation economy and society. It will encourage students to explore their pre-professional career identities as they explore the practical matters of study and employment options in health sciences.

Aims: This project is an evaluation of careers and employability learning (CEL) modules embedded in the Bachelor of Health Sciences curriculum. This project will evaluate the student experience of the modules and measure the degree to which they helped them begin to explore and develop graduate employability.

Key Scientific Skills: The student will receive training in aspects of teaching and learning including curriculum development, as well as training in quantitative and qualitative evaluation methods.

Further information: If you are interested in learning more about this project please contact either Brianna (B.Julien@latrobe.edu.au) or Louise (L.Lexis@latrobe.edu.au).

Project # 16: A novel antioxidant and anti-inflammatory approach to improve Type 2 diabetic heart function after acute myocardial infarction.

Supervisors: A/Prof Judy de Haan (Baker Heart and Diabetes Institute), Dr Daniel Donner (Baker Heart and Diabetes Institute), Prof Rebecca Ritchie (Monash Institute of Pharmaceutical Sciences), A/Prof Colleen Thomas (La Trobe University).

Background: Diabetic patients are at an approximately 30%-65% greater risk of developing heart failure (HF) after acute myocardial infarction (AMI) compared with non-diabetic patients, which is dependent on various risk factors prior to AMI. A significant risk factor includes the interaction of diabetes with hypertension. Preliminary data generated by the de Haan lab has shown augmented oxidative stress, inflammation and markers of heart injury in a novel diabetic and hypertensive mouse model. At a molecular level, the transcription factor Nrf2 plays a critical role in regulating oxidative stress, whilst sterile inflammation (a significant driver of CVD) is driven by the NLRP3-inflammasome. We hypothesize that targeting oxidative stress and inflammation via the recently identified Nrf2-NLRP3 inflammasome axis, will improve cardiac function post MI.

Aim: This study aims to prove that novel small-molecule activators of Nrf2, not only lessen oxidative stress but concurrently reduce inflammation, to improve diabetic cardiac dysfunction post AMI in a hypertensive setting.

Scientific Skills: Mouse microsurgery to induce MI. Assessment of cardiac function by high resolution ultrasound imaging (ECHO). Mouse dissections to obtain heart tissue. Gene expression analysis by RT-PCR, protein analysis by Western blotting. Immunohistochemistry and ELISA.

Further information: If you are interested in learning more about this project please contact Colleen (colleen.thomas@latrobe.edu.au). **Please note** - this research project will be undertaken and the Baker Heart and Diabetes Institute, Prahran, Melbourne.

Project #17: Characterising the role of Nedd4 gene in zebrafish heart development

Supervisors: A/Prof Colleen Thomas and Dr. Seb Dworkin

Background: The Nedd4 gene, highly expressed in the neural crest, regulates the formation of numerous organs in the mouse. Our interest lies in the role by which this gene regulates heart development. As congenital heart defects are one of the most common forms of birth anomalies, often persisting into adulthood and contributing to adult-onset heart disease, understanding the genetics of heart development is an important clinical approach to ameliorating the severity of these debilitating conditions.

Aims: Using the zebrafish as our model, owing to the well-established genetic tools and rapid embryonic development, this project will employ cutting edge technology to identify the role played by Nedd4 in heart formation.

Key Scientific Skills: This project will employ gene-knockdown, gene-deletion and gene-expression strategies in order to characterise the genetic mechanisms by which Nedd4 exerts its developmental function.

Further information: If you are interested in learning more about this project please contact either Colleen (colleen.thomas@latrobe.edu.au) or Seb (s.dworkin@latrobe.edu.au).

Project #18: Investigating the activity levels of patients with coronary heart disease enrolled in a dietary intervention trial.

Supervisors: Prof Michael Kingsley (La Trobe Rural Health), Dr Hannah Mayr (La Trobe University), Dr Jane Wilcox (La Trobe University), Prof Catherine Itsiopoulos (Murdoch University), A/Prof Colleen Thomas (La Trobe University).

Background: The AUStralian MEDiterranan Diet Heart Trial (AUSMED Heart Trial) is randomised controlled trial in coronary disease patients to determine the effect of 6-months Mediterranean diet vs. low-fat diet intervention on risk of secondary cardiac events. Although effect on physical activity (exercise) is not a target of the interventions, the study involves collection of activity data through both accelerometers and self-report surveys.

Aims: We have completed the pilot phase of the AUSMED in 65 patients. This Honours project will involve assessment of the collected activity data across 3 time points of the intervention (baseline, 3- months and 6-months) with the aims of (1) characterising the activity levels of this cardiac patient group (2) exploring relationships between activity levels and clinical measures, including biochemistry and body composition data, (3) determining the effect of dietary intervention on activity levels and (4) a comparison of activity levels as assessed by objectively measured accelerometers vs. self-report surveys.

Key Scientific Skills: An interest in clinical trials; particularly, exercise and dietary interventions. Computer analysis. All training will be provided.

Further information: If you are interested in learning more about this project please contact Colleen (colleen.thomas@latrobe.edu.au)

Project #19: Mechanistic investigation and novel therapy for cardiorenal syndrome

Supervisors: A/Prof Bing Wang (Baker Heart and Diabetes Institute) and A/Prof Colleen Thomas (La Trobe University).

Background: Cardiorenal syndrome (CRS) is a condition characterized by kidney and heart failure where failure of one organ worsens the function of the other, thus further accelerating the progressive failure of both. Current treatment options are sub-optimal for CRS and a better management strategy is urgently needed. It is known that uremic toxins (UT) accumulate in the setting of chronic kidney disease (CKD). We were the first to identify the direct detrimental cardiac effects of protein-bound UTs, including indoxyl sulphate, and have established both in vitro and in vivo models to study the mechanisms underlying the effects of UT in the cardiovascular system. Several pathways have been identified to be involved in the pathological process of CRS development.

Aims: This project will assess novel agents developed by our group targeting the pathways activated by UT, including oxidative stress and inflammation. This project is primarily laboratory-based, however, has direct clinical implications for the treatment of CRS.

Key Scientific Skills: The student will be trained in all procedures relevant to the project, including culture of cardiac and vascular cells. This may involve some animal surgery, histology/immunohistochemistry, as well as gene expression and protein assays of cell/tissue samples by qPCR and Western Blot. The student will perform the experiments under supervision, collect and analyse the data using quantitative methodology.

Further information: If you are interested in learning more about this project please contact either Colleen (colleen.thomas@latrobe.edu.au) or Bing (bing.wang@baker.edu.au). **Please note** - this research project will be undertaken and the Baker Heart and Diabetes Institute, Prahran, Melbourne.