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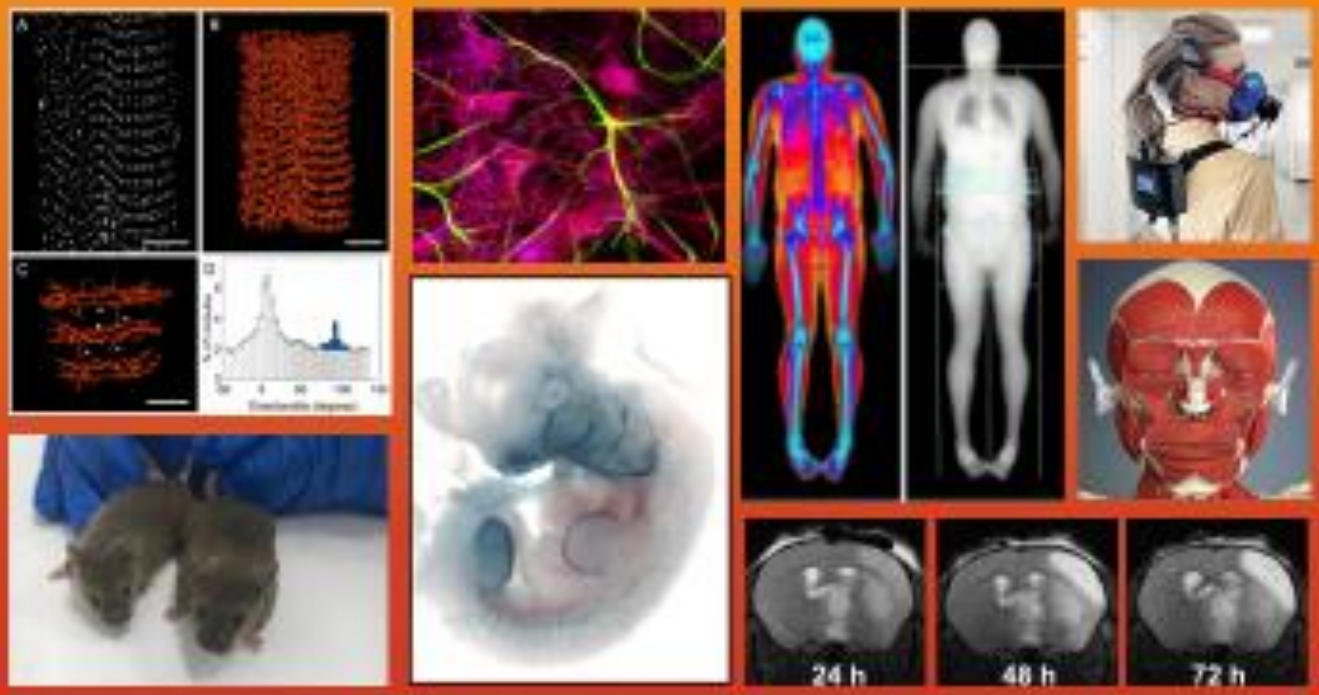
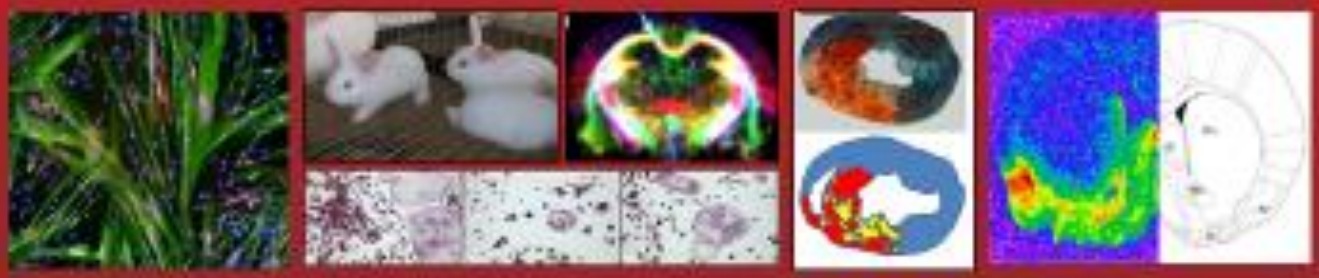


Department of Physiology, Anatomy and Microbiology

Honours in Physiology & Anatomy (HBS4HPA)



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Potential Honours projects in HBS4HPA 2019

Below is a list of projects that are being offered by the Department of PAM in 2019. 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: Investigating the impact that treatments for gestational diabetes have on maternal physiology and fetoplacental outcomes

Supervisor(s): Dr Tania Romano, Ms Kristina Anevska, Dr Jess Griffith (Uni Melb), Prof Mary Wlodek (Uni Melb)

Background: Gestational diabetes mellitus (GDM) is one of the most common pregnancy complications that has profound health risks beyond pregnancy for the child. As many women do not adopt healthy lifestyles

after GDM diagnosis, pharmaceutical treatments are often required. While commonly used clinically, the long-term effects of these treatments for GDM on child health are surprisingly unknown. Without knowledge of benefits or risks associated with these treatments for GDM on their child's short-term fetal and placental health, women are less likely to comply with taking pharmaceuticals during pregnancy, despite the short-term benefits for their health.

Aims: The aim of this project is to determine the impact that GDM treatments during pregnancy have on short-term (fetal and placental) outcomes.

Key Scientific Skills: The student will receive training in rat handling, weight and dimension measurement, glucose tolerance testing, insulin challenge testing, post-mortem, assays

Further information: If you are interested in learning more about this project, please contact Tania Romano (t.romano@latrobe.edu.au).

Project #3: Impact of high fat feeding and endurance exercise training in male rats born small has on cardiorenal and metabolic health

Supervisor(s): Dr Tania Romano, Ms Kristina Anevska, Dr Jess Griffith (Uni Melb), Prof Mary Wlodek (Uni Melb), Assoc Prof Glenn Wadley (Deakin)

Background: Many experimental and human studies worldwide have shown that babies born small for gestational age (or who are light at birth) are strongly and consistently at an increased risk of developing cardiovascular and metabolic diseases as adults, and that this risk is passed onto subsequent generations. Being overweight or obese can exacerbate these consequences. The relative role of paternal transmission is less well understood. We have demonstrated in our model of uteroplacental insufficiency that the fetal growth restriction is associated with hypertension, a nephron deficit and metabolic dysfunction.

Aims: The aim of this study is to determine whether the cardiorenal and metabolic phenotypes in males born small are exacerbated with high-fat feeding and whether endurance exercise can prevent the emergence of disaease.

Key Scientific Skills: The student will receive training in rat handling, rat treadmill exercise protocols, weight and dimension measurement, post-mortem, assays, pCR gene expression

Further information: If you are interested in learning more about this project, please contact Tania Romano (t.romano@latrobe.edu.au).

Project #4: Identifying the role of colostrum on organogenesis in the rat.

Supervisor(s): Dr Tania Romano, Ms Kristina Anevska, Dr Jess Griffith (Uni Melb), Prof Mary Wlodek (Uni Melb)

Background: In rats the early postnatal period is when organ development completes. During this period, the pups only source of nutrition is the mother. Despite the importance of the lactation period on the pup development, little is known of the impact colostrum versus mature milk on organogenesis, specifically within the kidney.

Aims: The aim of the study is identify the impact colostrum has on organogenesis in rats.

Key Scientific Skills: The student will receive training in rat handling, weight and dimension measurement, post-mortem, nephron number analysis, assays, pCR gene expression

Further information: If you are interested in learning more about this project, please contact Tania Romano (t.romano@latrobe.edu.au).

Project #5: Using Amnion Cells to Treat Ischemic Stroke (2 projects)

Supervisors: Prof. Chris Sobey, Dr. Helena Kim

Background: Stroke is the leading cause of death and disability and is usually due to an interruption of brain blood flow caused by the blockage of a cerebral artery by a blood clot. 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, and to promote long-term recovery. 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 now continue in mouse models of stroke: to 1) assess the effectiveness of hAECs in ischemic stroke in combination with a clot-buster drug (i.e. a thrombolytic); and 2) assess whether exosomes released by hAECs can also be used to effectively treat stroke in a cell-free manner. Exosomes are nanovesicles released by almost all cells and play important role in cell-to-cell interaction.

Aim: These projects will investigate the therapeutic effect of either hAECs in combination with a thrombolyitic or hAEC-derived exosomes in a thromobotic model of stroke and the impact on stroke-induced cognitive decline and/or motor impairment.

Key Scientific Skills: Students will receive training in thrombotic stroke surgery in mice, laser speckle imaging of brain blood flow, cognitive tests, histology, brain infarct size analysis, PCR for gene expression, immunohistochemistry for immune cell infiltration and inflammatory markers in mice following stroke.

Further information: If you are interested in learning more about this project, contact Prof. Chris Sobey **chris.sobey@latrobe.edu.au** or Dr. Helena Kim **helena.kim@latrobe.edu.au.**

Project #6:Does estrogen receptor signalling affect inflammation-driven injury following stroke?

Supervisors: Prof. Chris Sobey, Dr. Helena Kim

Background: Stroke is the leading cause of death and disability and is usually due to an interruption of brain blood flow caused by the blockage of a cerebral artery by a blood clot. Following stroke, inflammatory cells infiltrate the injured brain and contribute to secondary brain injury. Clinically, pre-menopausal women have a lower incidence and better outcome after stroke than men and post-menopausal women. Pre-clinical studies have reported a neuroprotective role of estrogen in the more severe model of stroke but the underlying mechanisms are not well understood. We have previously found that drugs selectively targeting a novel estrogen receptor (GPER1) can substantially influence stroke outcome in a sex-dependent manner. GPER1 is similarly expressed in males and females and so is potentially a relevant target for drug therapy in both sexes.

Aim: We have now established a colony of GPER-knockout mice and this project will utilize these animals to gain better understanding sex differences in outcome after stroke, in terms of brain injury and inflammation, cognitive decline and/or motor impairment.

Key Scientific Skills: Students will receive training in thrombotic stroke surgery in mice, laser speckle imaging of brain blood flow, cognitive tests, histology, brain infarct size analysis, PCR for gene expression, immunohistochemistry for immune cell infiltration and inflammatory markers in mice following stroke.

Further information: If you are interested in learning more about this project, contact Prof. Chris Sobey chris.sobey@latrobe.edu.au or Dr. Helena Kim helena.kim@latrobe.edu.au**.**

Project #7: 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 novel drugs with differing selectivity for inhibiting ROCK1 and ROCK2 have 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 (r.oshea@latrobe.edu.au).

Project #8:Sex differences in the development of aldosterone/salt-induced hypertension

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

Background: Hypertension affects at least 30% of the global adult population and is a major cause of stroke, myocardial infarction and chronic kidney disease. Aldosterone is a key regulator of blood pressure and consequently can contribute to hypertension. Sex differences in the incidence and severity of hypertension have been reported. Recent data from our lab suggests that the onset of aldosterone/salt-induced hypertension is delayed in female mice compared to male mice. Estrogen may have a protective role against hypertension however it is unclear what mechanisms are involved.

Aims: This project aims to determine mechanisms underlying sex differences in the development of aldosterone/salt-induced hypertension. Factors that can contribute to hypertension such as renal inflammation and fibrosis will be studied and compared in female and male mice.

Key Scientific Skills: The student will receive training in measuring blood pressure, minipump surgeries, flow cytometry, PCR 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: Characterising the role of adipose inflammation on obesity-related metabolic syndrome

Supervisor(s): Dr Maria Jelinic, Dr Antony Vinh and Prof Grant Drummond

Background: Obesity is a "low-grade" chronic inflammatory condition in which immune cells accumulate in various organs of the body to promote tissue damage, fibrosis and dysfunction. Obese individuals are also more likely to have metabolic syndrome (a collection of risk factors for that often occur together, including: hypertension, high blood triglycerides, hyperglycaemia or diabetes) and recent data suggests that different types of adipose tissue play different roles in the pathogenesis of these factors. We will use male 6-week-old C57BL/6 mice fed a high-fat diet for 10 weeks, to characterise the different adipose tissue types in a mouse model of obesity-related metabolic syndrome. Non-obese control mice maintained on a normal chow diet will be studied in parallel. Several *in vivo* physiological parameters will be measured on a weekly basis throughout the 10-week diet regimen including: body weight; food and water intake; blood glucose; renal function including albuminuria and creatinine clearance; blood pressure. Upon completion of the 10-week diet major organs (kidneys, heart, liver etc) and various adipose deposits will be harvested to examine the cellular composition and pro-inflammatory cytokine/adipokine profiles.

Aims: To characterise the cellular profile and pro-inflammatory factors within various fat deposits and determine the impact this has on major organs in obesity-related metabolic syndrome.

Key Scientific Skills: The student will receive training in mouse handling (incl. surgery, 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 Maria Jelinic (m.jelinic@latrobe.edu.au).

Project #10: Characterising metabolic syndrome and the microbiota in female mice on a high fat diet

Supervisors: Dr Maria Jelinic, A/Prof Ashley Franks, Dr Colleen Thomas.

Background: Having the right bacterial balance in our gastrointestinal system is important for good health. Alterations to the microbiota have been observed in a range of health conditions such as cardiovascular disease (including diabetes, hypertension and atherosclerosis). Dysbiosis of the gut microbiota may cause larger caloric intake (obesity is a risk factor for diabetes) and increased gut permeability (contributes to chronic low grade inflammation; also a feature of diabetes). We have a new mouse model of cardiometabolic disease, but the cardiovascular risk factors /profile and microbiome of the animals has not yet been characterised

Aims: Two complementary aims of this project will be to: (1) characterise the effect of a high fat diet on female mice from 6 weeks of age on blood pressure and blood glucose control and (2) evaluate changes in the composition of microbial communities present in the gastrointestinal tract as well as the gut histology.

Key Scientific Skills: Techniques to measure blood pressure and blood glucose levels will include tail plethysmography (tail cuff) and blood collections on live mice, and molecular analyses of the bacterial communities will include ARISA and qPCR (from faecal pellets). In addition, we will investigate changes to the gut histology to examine evidence of inflammation. All appropriate training will be provided.

Further information: If you are interested in learning more about this project please contact either Maria (m.jelinic@latrobe.edu.au), Ash (a.franks@latrobe.edu.au) or Colleen (colleen.thomas@latrobe.edu.au)

Project #11: The role of G protein coupled estrogen receptors in traumatic brain injury

Supervisors: Dr Stuart McDonald, Professor Chris Sobey, Dr Bridgette Semple (Monash)

Traumatic brain injury (TBI) is a leading cause of death and disability worldwide. There are no effective pharmaceutical treatments available for TBI, which is due in part to the incomplete understanding of the complex pathophysiology. With increasing evidence that TBI is a sexually dimorphic condition, there has been much interest surrounding the effects of sex hormones on TBI pathophysiology and their prospects as therapeutic targets to improve patient outcomes. Estrogen is one such hormone that may have neuroprotective properties following TBI, however, due to side effects of classical nuclear receptor activation in males, therapies targeting the recently discovered G protein-coupled estrogen receptor (GPER) may have broader therapeutic potential. Promising sex-dependent effects of GPER activation have been found following ischemic brain injury, however very little is known about the role of GPER activation following TBI. Accordingly, in this project, we will use a mouse model to investigate the role of GPER signalling in TBI. We hypothesize that the results from this study will provide novel insights regarding the suitability of GPER as a therapeutic target for improving TBI outcomes.

This project will involve animal handling and behavioural testing, molecular biology and biochemistry (e.g. real-time PCR, Western blotting, and biochemical assays). For further information, please contact Stuart McDonald (stuart.mcdonald@latrobe.edu.au) or Chris Sobey (c.sobey@latrobe.edu.au).

Project #12 : The effect of human amnion epithelial cells on traumatic brain injury outcomes

Supervisors: Dr Stuart McDonald, Professor Chris Sobey, Dr Bridgette Semple (Monash)

Traumatic brain injury (TBI) is a leading cause of death and chronic disability worldwide. Many TBI victims suffer from long-lasting cognitive deficits and other neurobehavioural disturbances. To date there are no pharmaceutical interventions that have proven effective in human TBI clinical trials, therefore it is imperative that new therapies are developed to improve patient outcomes. In this project, we will explore the therapeutic potential of intravenous injection of human amnion epithelial cells (hAECs) following an experimental TBI in mice. Professor Chris Sobey has recently discovered that intravenous injection of hAECs following experimental stroke in mice and marmosets results in a profound reduction in brain inflammation and injury and an improved long-term recovery. Given the significant overlap in neuropathological and functional deficits induced by ischaemic and traumatic brain injury, we hypothesise that hAECs will also improve TBI outcomes in mice.

This project will involve animal handling and behavioural testing, molecular biology and biochemistry (e.g. real-time PCR, Western blotting, and biochemical assays). For further information, please contact Stuart McDonald (stuart.mcdonald@latrobe.edu.au) or Chris Sobey (c.sobey@latrobe.edu.au).

Project #13 : The neuropathological and neurocognitive effects of concussions in athletes

Supervisors: Dr Stuart McDonald, Dr Brad Wright, Dr Sandy Shultz (Monash)

Concussion is a complex, presumed transient, disturbance to the brain that is induced by biomechanical forces. Although a single concussion rarely has lasting effects, there is some evidence that multiple concussions may be associated with the development of cumulative and progressive neuropathology and neurological impairments. These associations are preliminary and highly controversial; however, for individuals who are at high risk of experiencing concussions, such as military personnel and athletes, there is growing concern. In particular, amongst athletes, jockeys are known to be at the highest risk of suffering concussions, due to the nature of horse racing and the tendency for jockeys to have lengthy careers of near-daily riding. Nonetheless, very few studies have investigated the impact of concussions in jockeys. We believe that jockeys represent a

subset of athletes that may be able to provide invaluable novel insights into the potential long-term effects of concussions.

In this project, we will investigate the effects of a jockey's concussion history on several domains of cognitive function, as well as the blood levels of various biomarkers of neurotrauma and neuropathology. This project will involve cognitive testing and data analysis, as well as molecular biology and biochemistry (e.g. real-time PCR, Western blotting, and biochemical assays). For further information please contact Stuart McDonald (stuart.mcdonald@latrobe.edu.au) or Brad Wright (b.wright@latrobe.edu.au).

Project #14: Circulating microRNAs as biomarkers of concussion in athletes

Supervisors: Dr Stuart McDonald, Dr Caroline Taylor, Dr Sandy Shultz (Monash)

Current clinical management of concussion is guided by the presence or absence of symptoms, including physical, cognitive and emotional abnormalities. However, growing evidence indicates that symptom resolution does not indicate that the brain has recovered from the pathophysiological changes induced by concussion. Furthermore, there is also evidence that the adverse effects of repeated concussions are due to the recurring insults occurring before the brain has recovered from the initial concussion and is in a period of increased cerebral vulnerability. Currently there are no reliable markers that indicate when the brain transitions from this state of vulnerability, but the identification of such biomarkers would allow them to be used to guide medical decisions, so as to mitigate the potential long-term adverse effects of repeated concussions. In this project, we will explore the use of small non-coding RNA molecules known as microRNAs as biomarkers for concussion and recovery. The student will receive training in in sample collection/preparation, real time PCR, Western blotting, biochemical assays and data analysis.

Further information: If you are interested in learning more about this project please contact either Stuart (Stuart.McDonald@latrobe.edu.au) or Caroline (Caroline.Taylor@latrobe.edu.au).

Project #15: 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 and Prof Grant Drummond

Background: Abdominal aortic aneurysms (AAA) affect approximately 13% of the adult population aged over 65, and ruptured aneurysms can cause massive internal bleeding, which is usually 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 further inflammation in target cells such as T cells. Surprisingly, we have striking new data that IL-18R-knockout mice showed significantly greater incidence of AAA formation compared to wildtype (WT) mice using a mild model of AAA formation (KO: 87% vs WT: 9%). We now aim to further examine the mechanisms associated with the greater incidence in the IL-18R-KO mice. Firstly, we aim to address whether this phenomenon is also observed in an alternate model of AAA formation. We also aim to characterise the vascular structure and expression of extracellular matrix-degrading enzymes in IL-18R-KO mice compared to wildtype mice. 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 (a.vinh@latrobe.edu.au) or Grant (g.drummond@latrobe.edu.au).

Project #16: 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 #17: Vitamin D in ischemic stroke

Supervisor(s): Dr Michael De Silva, Dr Helena Kim and Prof. Chris Sobey

Background: Stroke is the leading cause of death and disability and is usually due to an interruption of brain blood flow caused by the blockage of a cerebral artery by a blood clot. There is now strong population-level evidence that vitamin D deficiency increases the risk of stroke, and the likelihood of a poor outcome following a stroke. It is not known how vitamin D levels might influence cardiovascular health before or after an event, nor is it known whether vitamin D supplementation can improve outcome measures.

Aims: This project will test whether vitamin D deficiency promotes cardiovascular risk factors and worsens stroke outcomes in mice. We will also test whether supplementation with vitamin D after stroke improves stroke outcomes.

Key Scientific Skills: The student will receive training in surgical procedures, assessing behavioural deficits, brain infarct size, 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 #18: High blood pressure and cognition: a role for the immune system

Supervisor(s): Dr Michael De Silva and Dr Antony Vinh

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, as well as biochemical (multiplex assays), 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 #19: Can Fucoidan improve skeletal muscle strength and endurance

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

Skeletal muscle is the largest organ in the human body and is the major site for energy expenditure. It exhibits remarkable plasticity in response to physiological stimuli such as exercise. Physical exercise remodels skeletal muscle and enhances its capability to burn calories, which has been shown to be beneficial for many clinical conditions including obesity, type-2 diabetes, metabolic syndrome, neurodegenerative diseases, cardiovascular diseases and cancer. While nothing can fully replace exercise, development of exercise mimetics that enhance or even substitute for the beneficial effects of physical exercise would be of great benefit. Fucoidan is a well-known bioactive compound of brown seaweed that anti-oxidative and anti-inflammatory properties.

This project will use a mouse model of aerobic exercise training along with multiple intraperitoneal injections of fucoidan, followed by *in vivo* and *in situ* functional assessment of skeletal muscle force and fatigue. Additional measures of the pathophysiology and effectiveness of fucoidan will include histological and biochemical (gene and protein) analysis of harvested tissues. This project will involve animal handling, animal procedures under anaesthetic and tissue dissections.

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

Project #20: Elucidating the protective role of interleukin-37 in kidney disease

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

Background: The kidney is the organ responsible for filtering out toxins from the blood, but also has many other important functions such as controlling blood pressure. Kidney damage is associated with significant inflammation that if sustained, leads to scarring and even complete kidney failure. Kidney inflammation is perpetuated though cells of the immune system that infiltrate the kidney and release pro-inflammatory cytokines. Interleukin (IL)-18 is one such cytokine and binding to its receptor, IL-18Rα that is expressed various immune cells including T cells, is known to promote inflammation. However, in response to another regulatory cytokine, IL-37, the IL-18Rα can also exert an anti-inflammatory response in humans. Therefore, this project will aim to determine if IL-37 is protective in hypertension and chronic kidney disease. To do this we will use a range of approaches including genetically modified mice, drugs that stimulate the IL-37 system and mouse models of kidney injury. By understanding these processes we may possibly identify new targets for therapies to lessen the burden of kidney disease.

Aims: To characterise the role of the IL-37/IL-18Rα-axis on chronic 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 #21: The functional role of miR-328 in brain injury

Supervisor(s): Dr. Caroline Taylor, Dr Jarrod Church and Dr Stuart McDonald

Background: MicroRNAs (miRNAs) are small, non-coding RNA molecules which are involved in RNA silencing post-transcriptional gene expression. MicroRNAs expressed in the blood of individuals and their expression profiles can be altered following a traumatic brain injury. Recent data from our laboratory has shown that miR-328 expression is upregulated in the circulation following a concussive injury. Whilst we are able to detect circulating miR-328, as yet we have no understanding of which cells in the brain are responsible for this increased expression, nor do we completely understand what its physiological role is.

Aims: This project will involve examining the expression and functional role of miR-328 in the brain under both physiological and pathophysiological conditions.

Key Scientific Skills: The student will receive training in cell culture and cell based assays, real-time PCR and immunocytochemistry.

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

Project #22: Characterisation of 3-dimensional constructs of muscle progenitor cells

Supervisor(s): Dr Caroline Taylor and Dr Jarrod Church

Background: Healthy muscle tissue is critical for a happy and healthy life, and when muscles are injured the loss of quality of life, and the burden on society, is significant. Tissue engineering offers exciting possibilities for enhancing the repair of skeletal muscle tissue. One approach has been the injection of muscle progenitor (stem-like) cells into injured muscle to assist with repair. Recent evidence suggests that progenitor cells in other tissues (e.g. liver) have far better rates of survival when cultured in 3-dimensional cell constructs ('spheroids') prior to implantation, possibly due to altered cell signalling (secretion of cytokines, growth factors, etc). To date, however, no studies have characterised the signalling changes in muscle progenitor cells formed into spheroids.

Aims: This project aims to investigate whether forming muscle progenitor cells into 3D spheroids alters the signalling profile of the cells, potentially enhancing their survival after implantation.

Key Scientific Skills: The project will primarily involve cell culture, real-time PCR, Western blotting, cell imaging, biochemical assays (e.g. ELISAs), and possibly some molecular biology (protein knockdown and/or overexpression).

Further information: If you are interested in learning more about this project please contact either Caroline (Caroline.Taylor@latrobe.edu.au) or Jarrod (j.church@latrobe.edu.au).

Project #23: Staff and student perceptions of a near-peer mentor program in undergraduate anatomy subjects

Supervisors: Dr Lloyd White & Heath McGowan

Background: The embedding of near-peer mentors into undergraduate anatomy practical classes may have benefits for the mentors, students and teaching staff. The near-peer mentor scheme involves the embedding of high-achieving 3rd year undergraduate human anatomy students (near-peer mentors) into weekly 2nd year undergraduate human anatomy practical classes, with the threefold aim of enhancing the learning experience for the 2nd year students, providing peer mentors with on-the-job leadership and communication experience, and assisting the teaching staff with the running of the classes. This study aims to assess the perceptions and opinions of students, near-peer mentors, and anatomy teaching staff regarding the near-peer mentor scheme. This research will assess the utility of the near-peer mentor scheme and allow for its improvement to better reflect the needs of all the parties involved.

Aims: This project aims to better understand the student, near-peer mentor, and teaching staff opinions regarding, and experiences of, a near-peer mentor scheme in second year La Trobe University anatomy subjects, with the aim of assessing its utility and effectiveness. It aims to answer the following specific research question: What are the benefits and pitfalls of a near-peer mentoring scheme?

a) from the perspective of the second year students

b) from the perspective of the near-peer mentors

c) from the perspective of the facilitators

This research will help inform the further development of the near-peer mentor scheme in anatomy at La Trobe University. It is intended that the findings of this project will contribute to a research publication.

Participants: Second year students in HBS2HAA and HBS2HAB; high-achieving third year students in HBS3HAC and HBS3HAD who have volunteered to act as peer mentors; practical class facilitators in HBS2HAA and HBS2HAB.

Data Collection: Surveys and interviews will be designed asking students, peer mentors and facilitators a range of questions relating to the peer mentor scheme (e.g. did they think it was useful?). Questions will be both closed (e.g. 5-point Likert scale) and open-ended in style.

A literature review will be undertaken to determine the known effects of near-peer mentoring schemes on student learning, and the student, mentor and facilitator perceptions of such schemes.

Data Analysis: Data from 5-point Likert scale style questions will be assessed quantitatively using means and standard error of the means. Responses to open-ended question will undergo content analysis to identify key themes regarding the near-peer mentor scheme.

Key Scientific Skills: The student will gain experience in both qualitative and quantitative research techniques. For data collection they may gain experience in the use of questionnaires, focus groups, interviews and databases. In addition, they may gain experience in difference analysis methods, including statistical analysis of quantitative data and thematic analysis of qualitative data.

Project #24: Students as Partners: evaluation of resources created to educate the public on the global health issue, hypertension

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

Background: Engaging students and staff effectively as partners in learning and teaching is arguably one of the most important issues facing higher education in the 21st century. Research shows that student engagement correlates with positive learning experiences and outcomes for students. Universities are increasing their focus on student engagement and experts are encouraging educators to provide students with opportunities to actively engage in their learning. One approach is to involve students as partners in learning and teaching; this includes through active learning, subject-based research and inquiry, and curriculum design. In 2017, a model of students as partners was piloted in which a team of students and academics was formed across Health Sciences and Media and Communications to work on creation of resources to inform the public on the global health issue, hypertension. The next step is to evaluate the effectiveness of the resources that were created in this project.

Aims: Evaluate the effectiveness of the resources created in a Student as Partners project to educate the public on the global health issue, Hyper10sion.

Key Scientific Skills: The student will receive training in aspects of education research, 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 #25: Open for Learning: an evidence-based approach to present the case for expanding open access etextbook creation at La Trobe University

Supervisors: Dr Brianna Julien, Dr Louise Lexis, Ms Fiona Salisbury and Professor Birgit Loch

Background: International, national and local evidence convincingly demonstrates the efficacy of open access etextbooks for student learning outcomes, experience and satisfaction. In 2017, The La Trobe eBureau was launched with three open access etextbooks written by La Trobe University (LTU) academics; these etextbooks were published as a partnership between LTU authors and the LTU library. Preliminary usage data indicates a high uptake of these etextbooks with over 2000 downloads since March 2017. As more teaching and learning is occurring in blended and fully-online contexts and students entering university today have access to and use devices including smartphones, laptops and tablets, it makes sense to provide students with resources intentionally designed for an online and blended learning environment. Open access etextbooks are available freely anytime and anywhere and this is particularly important for students at an economic disadvantage. LTU has a proud tradition of enrolling and retaining students from low socio-economic status (SES) backgrounds with participation rates higher than the state and national averages and plans to increase this population. Students from low SES backgrounds are particularly burdened by the high price of traditionally published textbooks.

Aims and outcomes: This project will investigate the following questions in a local context:

- How are the open access etextbooks produced by The La Trobe eBureau perceived by La Trobe students and academics?
- What are the institutional benefits and barriers to adopting widespread use of open access etextbooks at La Trobe?

At the conclusion of the project, a report will be produced that answers the project questions and makes evidence-based recommendations for expanding open access etextbook development at La Trobe. Most importantly, the outcome of the project will provide LTU academics with a roadmap for partnering with The La Trobe eBureau on the future production of open access etextbooks.

Key Scientific Skills: The student will receive 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 #26: Evaluation of an employability program embedded into the non-vocational Bachelor of Health Sciences course.

Supervisors: Dr Louise Lexis, Dr Brianna Julien, Mr Jason Brown and 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 currently has a sparse and piecemeal approach to the development of students' employability skills which are 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 design and introduce a scaffolded course-wide curriculum which will be integrated into targeted core subjects at each level and semester of the course. The curriculum will be 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 #27: Characterising the role of Nedd4 gene in zebrafish heart development

Supervisors: Drs Colleen Thomas and 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 #28: Investigating the ability of high polyphenol olive oil consumption to modulate cognitive performance

Supervisors: Dr Colleen Thomas, A/Prof. George Moschonis, Prof. Catherine Itsiopoulos.

Background: Extra virgin olive oil (EVOO) has been demonstrated to improve numerous cardiovascular disease outcomes. Recently, published clinical and animal studies have provided preliminary evidence to suggest that olive oil, as well as other polyphenol-rich interventions, may improve cognitive performance and prevent age- or experimentally-induced cognitive impairment.

Aims: In an industry co-funded study, we will be using a double-blinded randomised controlled cross-over trial design to recruit 50 healthy participants. The participants will follow a 3-week high polyphenol extra

virgin olive oil diet and a low polyphenol refined olive oil diet in random sequence, with a 2-week washout period in between. While other cardiovascular outcomes are being measured, this Honours project will focus on cognitive function and mood effects.

Key Scientific Skills: This clinical project can be tailored to a student's interests. It will have participant consult (food diaries, questionnaires, anthropometry) and dry lab (computer cognitive assessment battery) elements.

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

Project #29: Effect of Mediterranean Diet on citrus bioflavonoid compounds in the sera of patients with type 2 diabetes

Supervisors: Dr Hayder Al-Aubaidy, A/Prof Catherine Itsiopoulos, Dr Colleen Thomas.

Background: Citrus bioflavonoids are organic polyphenolic compounds with the capability of enhancing the absorption levels as well as the utilisation of vitamin C, and have been shown to possess both antioxidants and anti-inflammatory activities. Furthermore, we recently reported that these compounds may possess weak glucose-lowering properties. The healthy Mediterranean diet (MedDiet) is characterised by an abundance of plant foods (including fruit and vegetables) and a high habitual dietary intake of polyphenols. MedDiet has been demonstrated to improve the metabolic control of diabetes, but it is presently unknown if this dietary pattern modulates the major bioactive components of citrus bioflavonoids.

Aims: This project will involve analysis of serum samples collected from subjects with type 2 diabetes who consumed either an intervention diet (MedDiet) *ad libitum* or their usual diet for 12 weeks and then crossed over to the alternate diet. The primary aim will be to quantify the levels of various citrus bioflavonoid compounds in the sera of these participants (at baseline and follow-up) after each diet intervention to determine if MedDiet beneficially modulates their levels.

Key Scientific Skills: This project will involve basic chemistry skills, biospecimen sampling and handling. The major bioactive components of citrus bioflavonoids (naringin, hesperidin, and eriocitrin) will be measured using ultra-performance liquid chromatography. Data will also be correlated with other trial outcomes (eg., ability of MedDiet to improve glycemic control).

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

Project #29: Staff and student experiences, and student outcomes when comparing sole- and team-taught practicals in a first-year anatomy subject (HBS1HBB)

Supervisors: Heath McGowan, Dr Chris Silvester, Laura Whitburn and Dr Aaron McDonald

Background: Human Biosciences B (HBS1HBB) is a core first year (CFY) subject studied by over 2300 students from a variety of disciplines (Allied Health, Health Sciences & Biomedicine). This requires a large number of staff, both faculty and sessional, to facilitate classes. Student feedback on subject (SFS) surveys has revealed that the student experience differs due to variations in teaching styles and abilities. This is particularly the case at Bundoora, which has the highest enrolment numbers and therefore the greatest sessional staff requirements.

Therefore, a major change to the BU has been implemented in 2018 from a traditional format of

teaching (sole-taught) to a team-taught approach. Teaching teams comprise a Lead Demonstrator, and up to two Demonstrators with a staff:student ratio reduced from 1:30 to 1:20 -24. It is anticipated that students will have more contact with multiple staff, and staff interactions and mentoring will improve the skill-base and teaching consistency of all staff involved.

Aims: Specific aims of the study are:

1. To evaluate the effect of teaching format on students' learning experience by comparing the experiences of BU students (receiving team-taught) and regional students (sole-taught).
2. To quantify the effect of teaching format 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 in different formats.

This research will be used in the publication of an article on team-taught vs. sole-taught experiences at La Trobe University. The Honours project will be form part of this larger study. For example, the Honours project may only focus on either staff or student data, or on data from only one campus. This may be discussed and determined with supervisors.

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.Gowan@latrobe.edu.au) or Chris (C.Silvester@latrobe.edu.au).

Project #30: Investigating the activity levels of patients with coronary heart disease enrolled in a dietary intervention trial.

Supervisors: Dr Colleen Thomas, Prof Michael Kingsley, Dr Hannah Mayr, Dr Jane Wilcox, Prof Catherine Itsiopoulos.

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 trial 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 #31: Detection and monitoring of neuroinflammation by molecular imaging.

Supervisor(s): Prof. Karlheinz Peter (Baker IDI), Dr. Jacqueline Orian (LIMS) and Prof. Grant Drummond (PAM).

Background: Molecular imaging facilitates the identification and targeting of cellular processes, as well as monitoring of disease progression. The Peter laboratory has demonstrated the potential of this approach by the development of novel fluoroprobes with high specificity and sensitivity to platelets. These are tiny cell fragments that circulate in the bloodstream and are normally associated with clotting. They are also believed to play a major role in inflammation, but the nature of this role is still debated. A collaboration with the Orian laboratory, using the experimental autoimmune encephalomyelitis (EAE) model of multiple sclerosis, a neuroinflammatory condition, revealed two major findings. First, platelet accumulation was shown to precede that of inflammatory cells. Second, a cause-and-effect relationship between platelet accumulation and disease development was demonstrated. These findings represent a change in paradigm regarding mechanisms underlying neuroinflammation, but importantly, suggest a potentially therapeutically targetable mechanism to combat multiple sclerosis, with broader implications for inflammatory disease.

Aims: This project will combine molecular imaging and immunopathological approaches to obtain proof-of-principle that early targeting of platelets will facilitate disease monitoring and treatment in neuroinflammation.

Key Scientific Skills: The student will receive training in molecular imaging, immunopathology and the use of animal models to investigate human diseases.

Further Information: If you are interested in learning more about this project please contact either Karlheinz (Karlheinz.Peter@bakeridi.edu.au) or Jacqueline (J.Orian@latrobe.edu.au).

Project #32: 3D mapping of the cardiac cellular network

Supervisor: Dr Alex Pinto

Background: Recent advances in single-cell biology technology have advanced our understanding of the cellular composition of tissues and the role of cells in health and disease. Single-cell technologies have revealed that the heart comprises a diverse ecosystem of cells in which muscle cells are far outnumbered by support cells. While much information has been gained recently regarding the role of the non-muscle cells in heart function and the development of disease, we do not yet understand the spatial distribution of different cardiac cell types and the full extent of their physical interactions with one another. This project will aim to address this gap in our knowledge. Using single-cell RNA sequencing datasets, flow cytometry and 3D microscopy, this project will develop and use novel approaches for marking and spatially mapping distinct cardiac cell types. Understanding the distribution and physical interaction of cardiac cell types will advance our knowledge of how cardiac cells operate as a network and contribute to development of treatments which promote heart health and disease.

Aim: To map cardiac cell populations before and after tissue stress by combining 3D microscopy, single cell transcriptomic and flow cytometry approaches.

Key scientific skills: Preparation and analysis of samples by 3D microscopy and flow cytometry. Analysis of single-cell RNA sequencing data sets. Mouse handling and dissection.

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