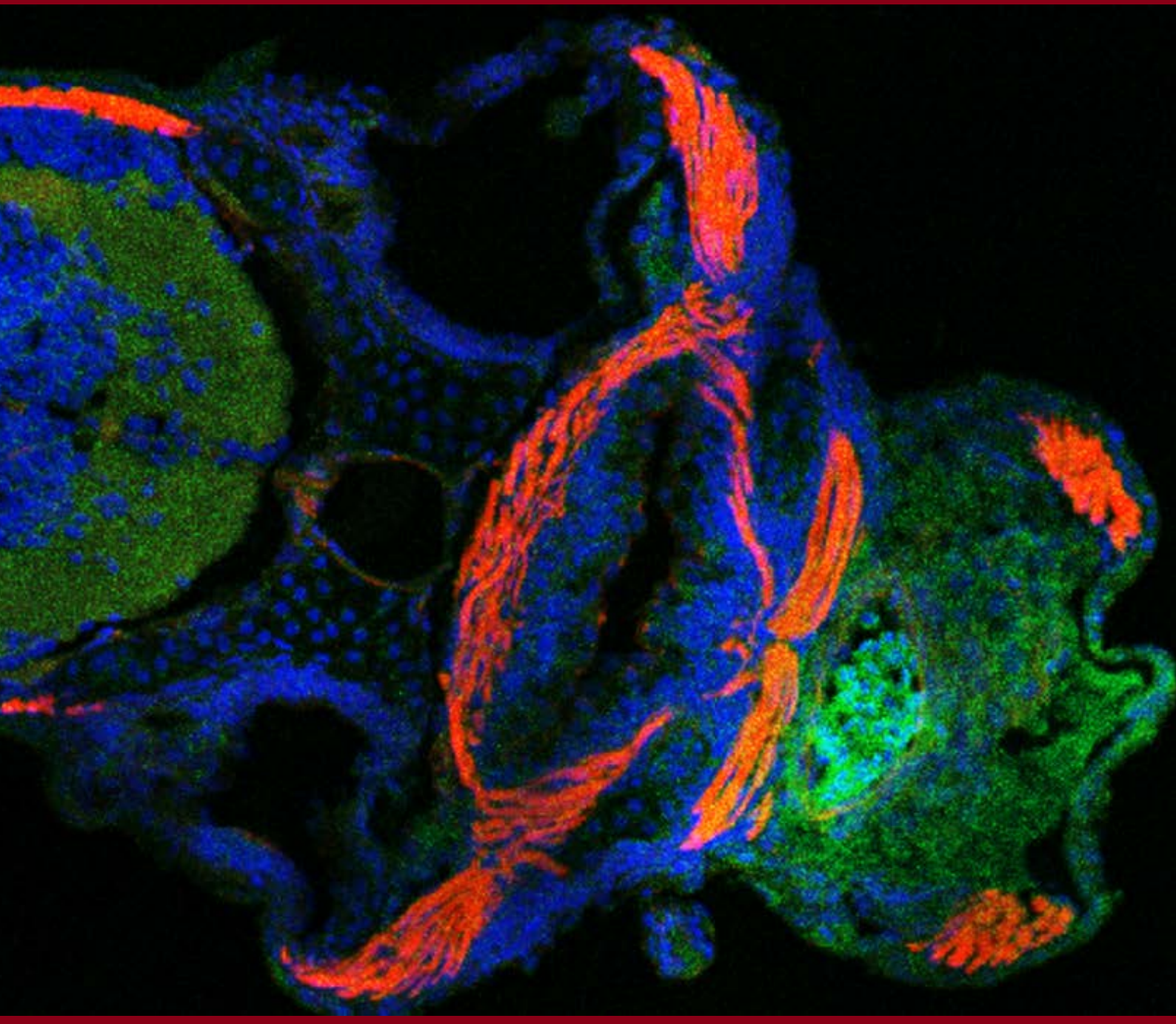
LA TROBE
UNIVERSITY • AUSTRALIA

Department of Microbiology, Anatomy, Physiology and Pharmacology

School of Agriculture, Biomedicine and Environment

Scientists at the forefront of knowledge into how biomolecules, cells, organ systems, disease and the environment interact to form functioning organisms (i.e. viruses, bacteria, animals, humans, etc.)



latrobe.edu.au/school-agriculture-biomedicine-and-environment

Contents

Cover Photo:
Expression of fibronectin in the anterior region of a zebrafish larva (Photo Credit: Nishanthi Mathiyalagan)

About the School of Agriculture, Biomedicine and Environment

The School of Agriculture, Biomedicine and Environment is one of the largest in the University, with more than 250 continuing and fixed term staff across multiple campuses. The School has seen significant growth in both research and teaching revenue. Staff in the School currently generate a significant proportion of the University's teaching revenue and research income, and supervise more than 230 higher degree research students. The School is responsible for 7 undergraduate degree courses at the main Bundoora campus in Melbourne, and our regional campus at Albury-Wodonga. It is a leader in teaching innovation and student satisfaction within the university.

The School undertakes teaching and research across a broad range of disciplines, including: Agriculture, Botany, Soil Science, Animal Science, Plant Science, Ecology, Environmental Geoscience, Evolution and Genetics, Conservation Biology, Zoology, Neurobiology, Microbiology, Physiology, Pathophysiology, Pharmacology and Anatomy, Biochemistry, Chemistry and Cardiovascular Physiology.

The 4 departments in the School are:

- Baker Department of Cardiovascular Research, Translation and Implementation
- Biochemistry and Chemistry
- Ecological, Plant and Animal Sciences
- Microbiology, Anatomy, Physiology and Pharmacology

The School of Agriculture, Biomedicine and Environment has recognised research expertise in biological, biomedical, environmental, molecular and chemical sciences. Our outstanding research environment gives academics access to the facilities and infrastructure needed to make significant discoveries.

We work collaboratively with our partners in industry, clinical organisations, philanthropy and government to achieve research outcomes that have a positive impact on the communities we serve.

We bring together the right capabilities, manage projects efficiently, act with integrity, and turn research results into translational outcomes.

Our contribution aligns with La Trobe's research themes: Healthy people, families and communities; Resilient environments and communities; and Understanding and preventing disease.

The School of Agriculture, Biomedicine and Environment research environment is dynamic and growing, and includes these major research centres:

- La Trobe Institute of Sustainable Agriculture and Food (LISAF)
- Centre for Cardiovascular Biology and Disease (collaboration with the Baker Heart and Diabetes Institute)
- Research Centre for Extracellular Vesicles
- Centre Research Biomedical and Environment Sensor Technology (BEST)
- La Trobe Institute for Molecular Science
- Research Centre for Future Landscapes (collaboration with the Arthur Rylah Institute of DELWP)
- Centre for Freshwater Ecosystems (formerly the Murray-Darling Freshwater Research Centre)
- Research Centre for Applied Alpine Ecology

Our staff are also members of these research centres:

- ARC CoE (Centre of Excellence) in Plants for Space
- Mallee Regional Innovation Centre (MRIC)(a joint venture with The University of Melbourne)

Professor Shaun Collin
Dean, School of Agriculture, Biomedicine and Environment, Co-Director of AgriBio

Department of Microbiology, Anatomy, Physiology and Pharmacology

The Department of Microbiology, Anatomy, Physiology and Pharmacology is one of the largest academic departments at La Trobe University. The Department consists of 50 continuing and fixed-term academic staff, including one Tracey Banivanua Mar Fellow, one ARC DECRA Fellow, and one NHMRC emerging leadership fellow. Professor Elly Djouma serves the role of Head of Department.

We teach >3000 undergraduate students enrolled across 32 subjects. We take great pride in providing a friendly and supportive environment, taking particular care to ensure a positive experience for undergraduate students.

We teach into La Trobe's undergraduate Science, Biomedicine and Allied Health ` and offer fully online subjects through Open Universities Australia. A number of our teaching staff have been recognised as Fellows/Senior Fellows of the UK's Higher Education Academy, and have received university and national awards for innovation and excellence in curriculum design and delivery.

Our Department produces graduates who are ready to take up a diverse range of job opportunities, with potential careers in government departments and agencies, hospitals, community health centres, rehabilitation centres, pharmaceutical and biotech companies, private health-care organisations and research centres.

The Department has a dynamic Higher Degree by Research (HDR) program that reflects the disciplinary interests of the staff. We are currently training 75 PhD and Masters students and 20 Honours (4th year Research) students from Australia and overseas.

Research carried out in the Department is world leading and focusses on some of today's biggest challenges in health and the environment. Staff and postgraduate students research the structure, function and environment of microbes, animals and humans in health and disease. Our breadth of expertise and co-location in world-class facilities create opportunities for new discoveries in cardiovascular biology and disease, neuroscience, developmental biology, musculoskeletal function, host-pathogen interactions and microbial ecology. Through this research, members of the Department are key contributors to La Trobe's new Research Themes of:

- Understanding and preventing disease
- A healthy, safe and equitable life course for everyone
- Production of quality foods and medicines
- Protection and restoration of vulnerable ecosystems

The Department's research activities also underpinned La Trobe University's ratings of '5 – well above world standard' in the latest round of Excellence in Research Australia (ERA) in the disciplinary areas of Physiology, Microbiology and Cardiovascular Medicine. The Department also contributed to similarly high ratings in the areas of Neuroscience and Soil Science.

The Department's research environment is dynamic and growing, and includes close relationships with world-renowned medical research institutes such as the Baker Heart and Diabetes Institute and the Howard Florey Institute of Neuroscience. We also have research partnerships with state, federal and non-government agencies, and are home to a major Research Centre:

- The Centre for Cardiovascular Biology and Disease Research

Research Centre

Centre for Cardiovascular Biology and Disease Research (collaboration with the Baker Heart and Diabetes Institute)

Centre for Cardiovascular Biology and Disease Research

Cardiovascular disease refers to chronic diseases involving the heart and/or blood vessels, often leading to heart attack, stroke, heart failure and kidney disease. Cardiovascular disease is also a major cause of dementia.

In Australia, 4 million people suffer from cardiovascular disease, costing the economy $5 billion annually. Alarmingly, cardiovascular disease claims more than 40,000 Australian lives per year, with the highest death rates amongst Aboriginal and Torres Strait Islander peoples, socioeconomically disadvantaged groups, and those living in remote and regional areas. It is for these reasons that cardiovascular disease is recognised as a National Health Priority area by the Australian Government.

There is an urgent need for more research and greater public awareness to address the enormous health and economic impacts of cardiovascular disease.

The Centre for Cardiovascular Biology and Disease Research was established in 2018 by Professors Chris Sobey and Grant Drummond. In just five years, the Centre has attracted more than $13 million in research funding and is now home to more than 75 research staff and students, making it one of the largest cardiovascular research groups in Australia.

Our researchers utilise leading animal, organoid and cell culture models, and cutting-edge technologies including mouse genetics, physiology, immunology, single cell and spatial transcriptomics, proteomics, microbiomics and molecular imaging. This enables translation of discoveries into novel diagnostics, preventions and treatments for cardiovascular disease.

Our experimental findings on cell therapy in stroke have recently been translated into Phase I and Phase II clinical trials.

Our Centre is located in the heart of Melbourne's northern suburbs, serving a community that is disproportionately impacted by the devastating consequences of cardiovascular disease and stroke. Our researchers work closely with the local community through public awareness campaigns, high school education programs, and partnerships with local government, health care providers and industries. The Centre also seeks input from members of the local community for strategic decision making, research planning and dissemination of findings.

Co-Directors:
Profs Chris Sobey and Grant Drummond
(c.sobey@latrobe.edu.au)
(g.drummond@latrobe.edu.au)

Research Divisions and leaders:
Cardiac Cellular Systems
(Associate Professor Alex Pinto)

Cardiac Disease Mechanisms
(Dr James Bell)

Cardiorenal Disease
(Dr Brooke Huuskes)

Cardiovascular Physiology
(Associate Professor Colleen Thomas)

Cerebrovascular Disease
(Dr Michael De Silva)

Diabetes Development and Prevention
(Associate Professor Hayder Al Aubaidy)

Dying Cell Communication and Clearance
(Dr Amy Baxter)

Hypertension and Diabetes
(co-led by Associate Professor Antony Vinh & Dr Maria Jelinic)

Immunometabolism and Macrophage Biology (Dr Katrina Binger)

Microbial Genetics and Interactions
(Associate Professor Steve Petrovski)

Molecular Proteomics
(Dr David Greening)

Stroke and Brain Inflammation
(Dr Helena Kim)

Vascular Therapeutics and Regeneration
(Dr Kazuhide Shaun Okuda)

Strategic Partners:
Australian Cardiovascular Alliance,
Baker Heart and Diabetes Institute,
CAD Frontiers, and
Beluga Foundation.

Research Groups

Anatomical Sciences and Higher Education Research Group

Anatomy ('to cut up') is the study of the structure of an entity.

Therefore, Human Anatomy concerns itself with the study of how the human body is structured.

It is often said that there is nothing new to discover about the human body.

For hundreds of years, it was believed that we know how many muscles and bones and organs we have.

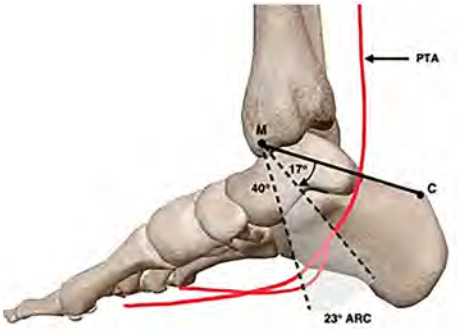
Therefore, there must not be much more to study!

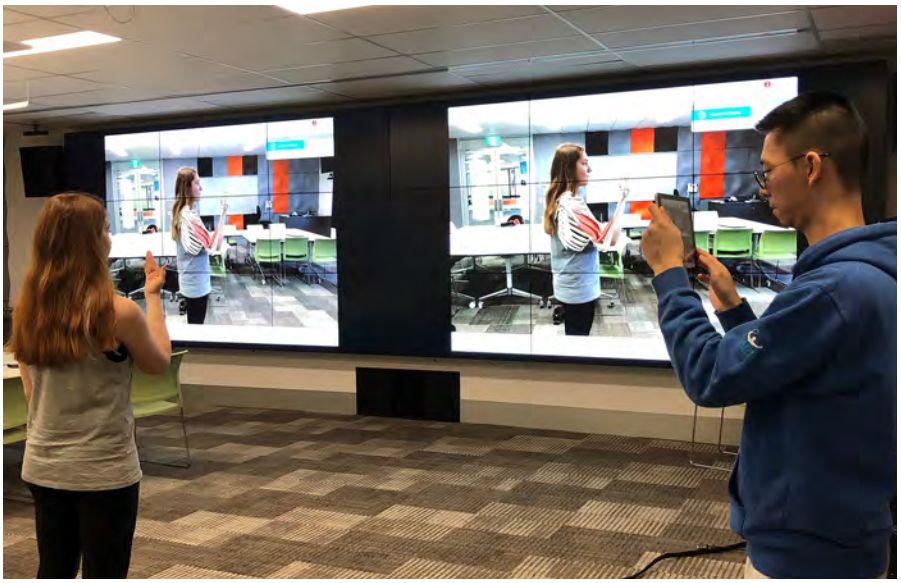
However, anatomical research continues to make new discoveries about the human body, such as identifying new structures previously unknown (e.g. there are actually five muscles forming the 'quadriceps femoris' group, and there are lymphatics in the brain when previously it was thought there were none).

These new findings are helping to improve medical interventions such as surgical techniques, as well as the functional and clinical understandings contributing to health and disease and injury management.

Additionally, studying Human Anatomy is considered one of the most challenging topics in a science degree.

Helping students develop meaningful ways to study and apply their anatomical knowledge is essential.





Anatomical education has evolved significantly since the days of the didactic 'sage on a stage' lecture.

Although students think they learn more by watching a good lecturer up on stage, they ultimately understand less when compared to those engaged in active learning activities.

Our research group is interested in both anatomical science research (focused on better understanding the anatomical relationships in the body and their clinical applications) and developing and evaluating better ways to teach and learn anatomy.

In combination, these areas of focus ensure that students are being taught the most current anatomical information and are also being taught using evidence-based, contemporary teaching and learning methods.

GroupHead:
Assoc Prof Aaron McDonald
(a.mcdonald@latrobe.edu.au)

Group Members:
Dr Laura Whitburn
Dr Heath McGowan
Dr Brooke Huuskes
Dr Narbada Saini
Dr Jency Thomas
Ms Melby Tentrisanna
Mr Shane Cassar
Ms Frances Deen

Fields of Study:
Gross anatomy; topographical anatomy; higher education research in human anatomy.

Capabilities and Techniques:
Human dissection; ultrasound; qualitative and quantitative analysis; digital educational technologies; curriculum development; student-teacher co-creation; peer-peer learning.

Translational Opportunities:
Education; curriculum development; human dissection; sports and exercise science; medical research.

Antiviral Innate Immunity Group

Viruses infect all living organisms. Our laboratory studies both viruses of animals and humans to unravel the role of novel host and viral proteins in the control of viral infection, with a goal towards development of novel strategies to combat viral infection in both humans and animals. Our group uses advanced imaging, molecular, and genomic techniques to perform research across 2 main themes: (1) Host Induction of an efficient antiviral response and (2) Control of viral pathogens.

Theme 1: Host Induction of an efficient antiviral response
When a virus infects a cell, the host cell has sentinel receptors to detect foreign viral material. Receptor activation triggers a cascade of signaling pathways resulting in the upregulation of interferons, the main antiviral cytokines, which further upregulate thousands of antiviral gene products. Limited drugs are available to treat viral infections, and many significant viral infections have no treatments other than supportive care. We study molecular mechanisms that underpin the ability of a host cell to upregulate the most effective antiviral response. We focus on multiple viral pathogens across many animal and human models to uncover novel pathways and host proteins that will assist in developing next generation anti-viral drug treatments for multiple viruses.

Lipid droplets (LDs) as a novel antiviral target
Our group has recently demonstrated that the lipid droplet (LD) is an essential organelle in facilitating an efficient and robust antiviral response for the first time. LDs contribute to key pathways important for the physiology of cells. In a homeostatic view, they regulate the storage of neutral lipids, facilitate removal of toxic lipids, and are involved in cellular communication. Recent advances in the field show these organelles are essential for cellular stress response mechanisms, including inflammation and immunity, with LDs acting as hubs to integrate metabolic processes.

Lipid droplets inside mosquito ovaries. (Photo credit: Ebony Monson)

Changing proteome/lipidome of LDs Recent attention has focused on LDs because of their ability to rapidly change their proteome and our team has described the changing LD proteome during viral infection for the first time. We can isolate LDs from tissues and cells and have developed methods to separate out the proteins and lipids from the LDs giving us a very unique analysis pipeline to examine individual lipids and proteins using advanced mass spectrometry methods on the LD during virus infection.

Development of artificial LDs (aLDs)
We have now developed a pipeline to make aLDs in collaboration with Prof Adam Mechler's group (BC, LIMS) and are developing these aLDs as a novel antiviral strategy for the first time.

Theme 2: Control of viral pathogens
Viral pathogen control is solely restricted to vaccines in the veterinary sector, with vaccines and a small handful of drugs available for the treatment of some viral infections in humans. In collaboration with the Prof Travis Beddoe's Group (APSS) we work on developing new vaccines and tools to run vaccine trials for the veterinary sector. We focus on solutions for viral pathogens in small aquatic animals, where they do not have an adaptive immune system, and rely on innate immunity to control viral pathogens. We use our host induction research to develop new immune priming strategies to target viral pathogens in the aquatic livestock industry.

Lab Head: Prof Karla Helbig (k.helbig@latrobe.edu.au)

Lab members: Dr Ebony Monson; Ms Irumi Amarasinghe; Ms Zahra Telikani; Ms Jacinta Agius; Mr Darcy Beveridge, Mr Garry Chahal, Mr Lachlan Ridgeway, Mr Lachlan Wallace

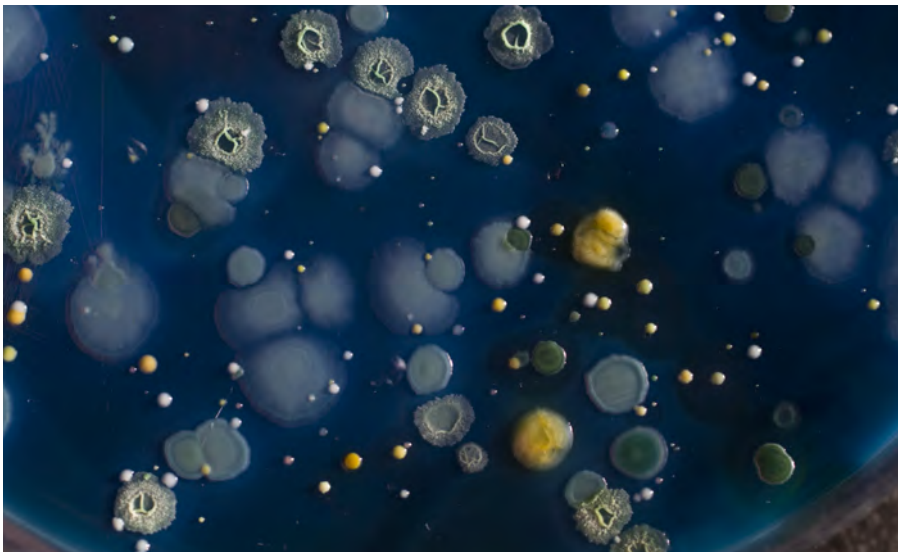
Fields of Study:
Virology; Innate Immunology; Immunity; Lipid droplet biology; Lipids; Veterinary pathogens.

Capabilities and Techniques:
High end microscopy including confocal, super resolution, light, fixed, live cell & imaging of complex tissue types (brain, lungs, and mosquitos); Cell & virus culture & propagation; Primary cell culture; Animal husbandry (mice/abalone); Viral delivery of genetic material; CRISPR/ cas; High sensitivity proteomics and lipidomics; Lipid droplet isolations; Protein expression & purification; Next generation sequencing; General molecular biology (ELISAs, western blotting, RT-qPCR etc.).

Translational Opportunities:
Viral animal pathogen detection; Targeted drug development and management; Characterisation & modulation of innate immune responses; Development of novel antiviral therapeutics; Vaccine/ immune priming design/ delivery.

Applied and Environmental Microbiology Group

Our research investigates a diverse range of microbiomes associated with soil, human and ecosystem health. We have in-house Illumina Next-Generation sequencing facilities and develop custom bioinformatic pipelines for structural and functional community analysis. We have custom made equipment for the study of anaerobic microorganisms including electroactive bacteria, gut and soil microbes. We collaborate with medical, soil science and ecology researchers as well as NGOs, corporate partners, landholders, national and international partners. We lead the microbial branch of the La Trobe Applied Microbiomes project (LAMP) and pioneer the use of functional traits in microbiome research.



Culturing diverse microorganisms (Photo credit: Gene Drendel)

Pioneering trait ecology in microbiome analysis

From soil to human health, there is an urgent need to predict how changes to microbial community structure impact community function. We pioneer the use of functional traits to study microbial communities and how they impact environment functions. Traits go beyond looking at 'who' is present in a community, to understanding 'how is the community behaving', leading to identifiable opportunities for 'engineering' these communities for beneficial outcomes in health, disease and environmental research.

The human microbiota in infant health

The human microbiota contains trillions of microbial cells with most present in the gut. Branched chain fatty acids (BCFA) in breast milk influence normal human microbiota development, infant gut epithelial cells, and the immune system. Preterm infants and those mainly fed on formula often lack BCFAs. We isolate bacteria producing BCFAs to study their impact on human microbiota and gut health. Our research may lead to new infant formulas for optimal infant gut and microbiota development.

The microbiome in health and disease

The human microbiome, performs vital health functions that influence immunity, synthesis of essential molecules, and even our mood. Interactions between the microbiome, genetics and physiology are complex. We collaborate with clinicians, neurobiologists and physiologists to study the microbiome's role in Parkinson's disease, Autism and other disorders.

Promoting ecosystem health from the ground up

Agricultural and natural ecosystems rely on soil microorganisms to drive key ecosystem functions. For example, microorganisms are gatekeepers of the carbon cycle, both creating and removing carbon from soil systems. We study how the ecology of a microbial community governs these key ecosystem services, the wider implication for ecosystem function and interactions with climate. The answers to these questions have far reaching implications for the role of soil health in ecosystem restoration and sustainable farming and climate change mitigation.

Applied electromicrobiology

The developing field of electro-microbiology investigates bacteria with novel electrical properties including the ability to transfer electrons between each other and onto stable surfaces such as electrodes. We use microbial fuel cells
(MFCs) and plant MFCs to study these electroactive microbes and key roles they play in corrosion in bioremediation processes.

Rare and extreme microbiomes

We study microbial survival in extremeenvironments to understand the role of microbes in biogeochemical cycling, primary production and as mediators and mitigators of climate change.

Lab Heads: Dr Jennifer Wood (jen.wood@latrobe.edu.au) and Prof Ashley Franks (a.franks@latrobe.edu.au)
Lab Members: Dr Anya Shindler (senior researcher); Mr Luke Bosnar; Ms Berenice Della Porta; Ms Edden Subejano; Ms Lauren Haylen; Ms Nadia Zermani; Mr Kyle Iseppi; Ms Urja Amin.

Fields of Study:
Microbiology; Ecology; Health; Bioremediation; Soil Science.

Capabilities and Techniques:
Next-generation sequencing, quantitative PCR; Anaerobic microbiology (gassing station & anaerobic chamber); Electro-microbiology; Trace gas analysis; multivariate statistics; bioinformatics.

Translational Opportunities:
Early detection/alleviation of human disease phenotypes (in Parkinson's Disease & Autism); improved sustainable agricultural land management practices; holistic ecosystem conservation and monitoring; soil contaminants bioremediation.

Cardiac Disease Mechanisms group

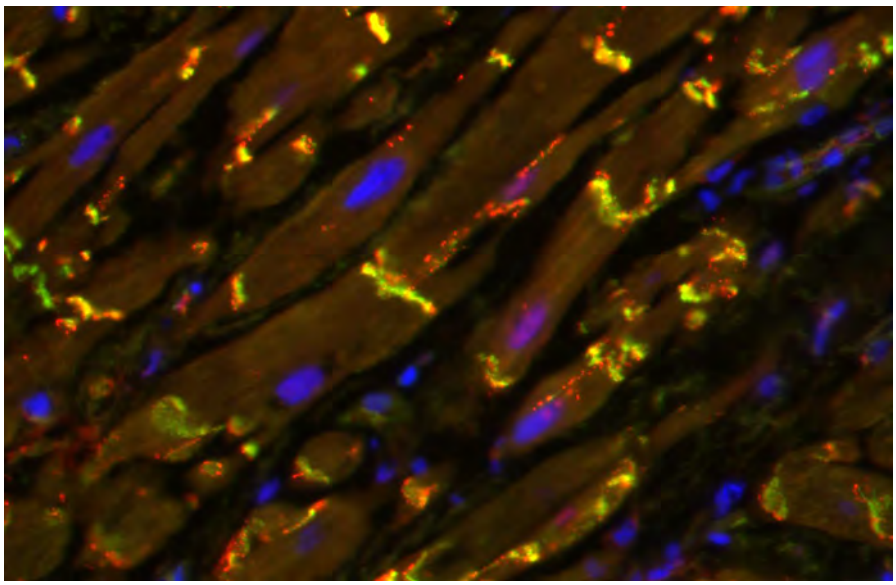
The Cardiac Disease Mechanisms Laboratory seeks to understand the cellular and molecular mechanisms driving diseases in the heart in a bid to identify new candidate targets for future therapies. One in five of all deaths in Australia are due to heart disease – a devastating public health and economic burden that will continue to escalate with an increasingly aged and obese population. This new research group within the Department has extensive expertise in in vivo, in vitro and molecular methodologies, with a focus on examining the underlying causes and pathological consequences of irregular heart rhythms (arrhythmias), heart attacks (myocardial infarction) and chronic heart failure.

'Heart fat' emerging as a critical mediator of heart disease

Increased body fat (especially visceral tummy fat) is known to be an important contributor to the development of heart disease, releasing factors into the blood that travel to the heart and disrupt function. Up until recently though, the role of the fat immediately surrounding the heart has been largely overlooked. This 'heart fat' increases markedly in obesity, with aging, and in post-menopausal women – all important risk factors for heart disease. Heart fat is increasingly thought to be critical to the development of irregular heart rhythms and relaxation abnormalities that represent a primary component of cardiac demise.

Inter-cellular communication between heart fat and muscle cells drive irregular heart rhythms

We have very recently shown that heart fat exerts a unique, detrimental influence on the surrounding heart muscle. Our findings show that the very close proximity between the fat and muscle cells within the heart greatly increases the potential influence of this local fat on heart function. We have taken the first steps in identifying the factors released from the heart fat, and look to establish how these modulate the function of neighbouring heart muscle cells in a manner that increases their vulnerability to potentially fatal irregular heart rhythms.



Cell-to-cell communication proteins in human cardiomyocytes (Photo credit: Jim Bell)

Relaxation abnormalities in fatty hearts?

We are also taking the field in a new direction, by investigating a very recently described clinical link between heart fat and the capacity of the heart to relax. An inability of the heart to relax properly disrupts its capacity to fill with blood, and is an emerging global health issue with no effective therapies available. Building on our growing understanding of the factors released from heart fat that influence heart rhythmicity, we seek to also identify how these may drive relaxation abnormalities that eventuate in heart failure and death.

Our research capacity is supported by ongoing pre-clinical/clinical collaborations developed both locally (University of Melbourne, Baker Heart Institute) and internationally (University of Birmingham, UK).

Lab Head: Dr Jim Bell (j.bell@latrobe.edu.au)

Lab members:
Sarah Hayes; Hamish Lindstrom.

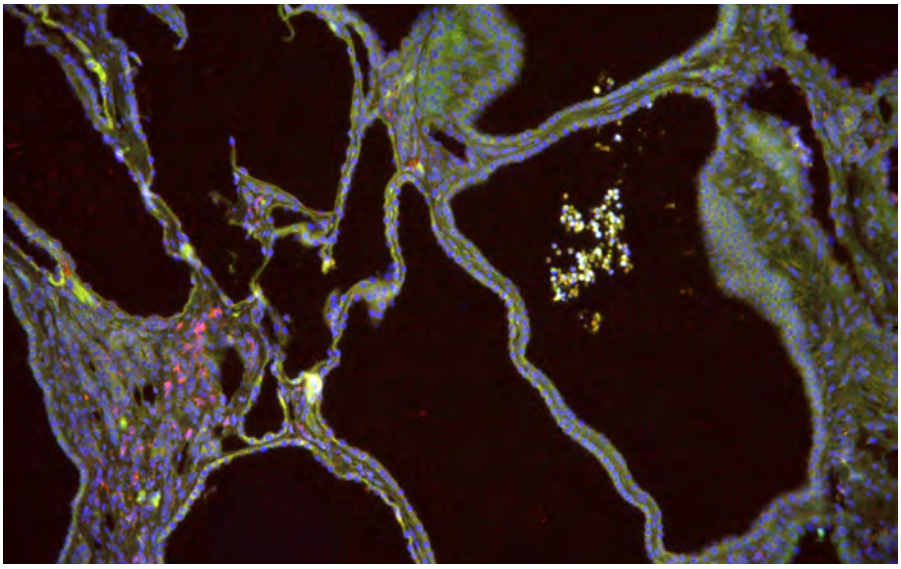
Fields of Study:
Cardiac arrhythmias; Heart failure; Adipose tissue; Intercellular signalling; Sex steroids.

Capabilities and Techniques:
Human cardiac tissue collection & rodent models of obesity; isolated heart & cardiomyocyte contractility; electrophysiology & conduction mapping; protein biochemistry; fibrosis/adipose infiltration quantification.

Translational Opportunities:
This research will identify novel molecular targets that advance preventative therapies for aged and obese populations at risk of developing heart disease.

Cardiorenal Disease Research Group

Kidney disease affects around 12% of the population and places a huge burden on the individual suffering the disease. The only option for patients is dialysis or transplantation. Dialysis is life limiting and there is a sever organ shortage meaning long wait times for those in need. Devastatingly, people with kidney failure often die of a cardiovascular event before even getting a lifesaving transplant. Imagine a world where we can completely reverse the effects of kidney disease. That is the goal of the Cardiorenal Disease Research Group, to unravel the mysteries of chronic kidney disease and find new ways to stop the progression of this disease, and even regenerate the kidney. Further, we are using qualitative research methods to understand how transplant recipient experience the public health system and also investigate how to increase the number of organ and tissue donors in Australia.



Macrophage staining in polycystic kidney disease. (Photo credit: J. Gasperoni)

Does the immune system contribute to polycystic kidney disease progression?
Polycystic kidney disease (PKD) is a genetic condition affecting up to 1in 400 people worldwide. This inherited condition comes in two forms: Autosomal Dominant (ADPKD) and Autosomal Recessive (ARPKD). Patients with PKD grow large fluid filled cysts on their kidneys which causes several side effects due to the crucial role that the kidneys have in maintaining body homeostasis. Namely, the cyst grow so big that they destroy the kidney tissue, eventually leading to complete kidney failure. One major side effect of PKD that patients have high blood pressure.
Using both zebrafish and rodent models of, we aim to understand how the immune system contributes to disease development, progression and high blood pressure. By identifying the molecular pathways involved in disease progression we may be able to design therapies to stop disease early in its progression.

Can Zebrafish be used to screen for new drugs to treat kidney disease?
Zebrafish develop cystic changes in a way that is similar in humans. This gives us the unique opportunity to screen new compounds that may be beneficial in stopping or slowing the progression of PKD development. Zebrafish embryos are transparent and develop outside the body, so we can use sophisticated microscopy techniques to monitor their development in real time.

Why do cells dye in human kidney disease?
We use new technology called tubules on a chip (TOAC) to understand the crosstalk between cells of the kidney and the immune system.
In this cell culture technique, we take cells from human kidneys, which have been surgically removed from patients with kidney cancers or PKD, and grow epithelial cells in one chamber, endothelial cells in another. We then add immune cells and culture everything under physiological flow, meaning that this culture method closely represents what occurs in the human kidney. Using Bulk RNA sequencing, we can determine the cellular changes that occur under different conditions, giving us insight into the cellular changes associated with disease progression.

How has telehealth changed the way care is delivered to kidney transplant patients?
This qualitative study will expand on our recent work that looked into how kidney transplant recipients feel about using technology in their post-transplant care. The results of this previous study was used to lobby for government changes into telehealth services across Australia. Now, we want to gain insight into the physicians point of view and determine if the mode of healthcare delivery affects patient outcomes.

Lab Head: Dr Brooke Huuskes
(b.huuskes@latrobe.edu.au)

Lab members:
Emily Major, Sean Barton, Emily Dixon.

Fields of Study:
Kidney disease, Hypertension, Genetics, Public Health, Patient-centered

Capabilities and Techniques:
Animal models of kidney disease (including rodents and zebrafish), molecular biology techniques, human cell culture, live-cell imaging, histopathology, immunohistochemistry, confocal microscopy, renal function, qualitative data collection

Translational Opportunities:
Understanding the mechanisms involved in kidney disease allows us the opportunity to identify new therapies for kidney disease. Through qualitative research, there is opportunity to impact current practices in government processes and policy.

Cerebrovascular Disease Group

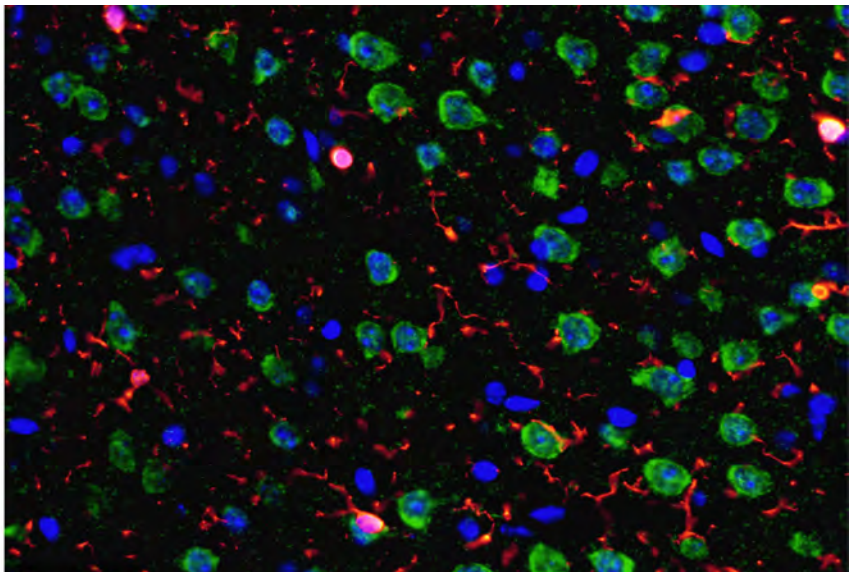
Cerebrovascular diseases (stroke, dementias) are a major health concern in Australia and throughout the world. The brain is and its circulation are particularly sensitive to disease. Cardiovascular diseases disrupt the function of cerebral arteries which leads to a dysregulation of cerebral blood flow. This may lead to altered blood flow to the brain which may starve neurons of the continuous supply of oxygen and other nutrients essential for their function. Insufficient delivery of oxygen and nutrients to the brain is a major factor in neuronal dysfunction and may contribute to the development of cognitive impairment (e.g. loss of memory). Our research focuses on the effects on cardiovascular diseases (e.g. hypertension, ischaemic stroke, metabolic syndrome) on the brain and its circulation. We utilise animal models of disease as well as state of the art imaging, molecular and behavioural testing techniques to determine the impact of disease on the brain and identify potential targets for therapy.

Targeting estrogen signalling to reduce dementia risk

It was recently reported that postmenopausal women with hypertension to have the greatest reduction in brain health between ages 60-80. This decline is greater than in groups regarded as "unhealthier" (e.g. males with multiple cardiovascular diseases). Loss of protection by estrogen after menopause is a likely contributor. We have shown that activation of the G protein-coupled estrogen receptor (GPER) is protective in cardiovascular disease models, including hypertension and stroke. Importantly, selective activation of GPER avoids unwanted effects that result from activation of classical estrogen receptors. In this project we will study menopause-accelerated brain atrophy and cognitive decline in female mice with hypertension and if these changes to brain health can be prevented by pharmacological targeting of GPER.

Comorbidities and stroke

Stroke patients are typically older and have one or more cardiometabolic diseases. Despite this, most preclinical research is performed in young, healthy animals.



Staining for neurons and microglia in the prefrontal cortex. (Photo credit: Tarunpreet Rajput)

This has likely contributed to the failure to translate drugs identified in preclinical studies to clinical use. Hypertension is the major risk factor for stroke and we recently found that hypertension worsens memory after stroke. The combination of hypertension and stroke altered the transcriptomic profile of the brain, with changes to genes associated with neuroinflammation and neuronal function. This project aims to understand how hypertension, or other cardiometabolic diseases, worsens stroke outcomes.

Human amniotic epithelial cells and cognitive function

Cardiovascular diseases are known to promote brain injury and may therefore, result in impairment of cognition. The complex mechanisms that underly these diseases mean that a single therapeutic agent is unlikely to be effective. Human amnion epithelial cells (hAECs) have many properties (eg. anti-inflammatory, antifibrotic, regenerative and immunologically inert) that make them attractive candidates for a cell-based therapy for disease. This project will determine whether hAECs can treat cardiovascular disease-induced brain injury and cognitive impairment.

Lab Head: Dr Michael De Silva (tdesilva@latrobe.edu.au)

Lab members:
Dr Quynh Nhu Dinh; Mr. David Wong Zhang; Mr. Yeshwanth Yeraddu; Mr. Louis Tran.

Fields of Study:
Dementia, stroke, vascular function, brain injury, behaviour.

Capabilities and Techniques:
Animal models of hypertension and stroke; flow cytometry; histopathology; immunohistochemistry; confocal microscopy; genomic sequencing; mouse behavioural/cognitive testing; oxidative stress & inflammation assessment; vascular reactivity/ compliance.

Translational Opportunities:
New drug targets: Pre-clinical dementia/ stroke.

Developmental Genetics Group

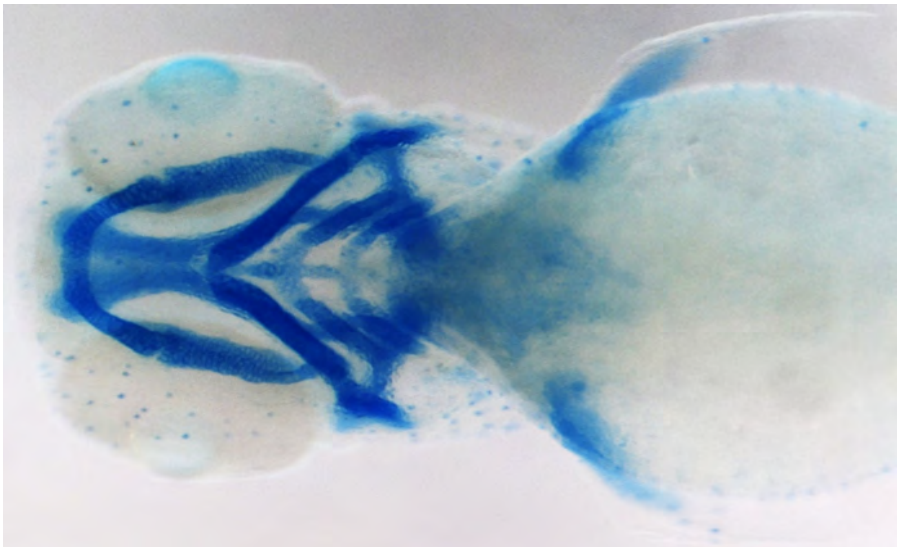
Understanding the cellular behaviours, particularly in the craniofacial region and neural tube, and the molecular pathways by which these behaviours are regulated, forms the cornerstone of understanding embryonic development. Using genetically-modified mouse and zebrafish models, our group identify critical genetic networks that underpin formation of the head (brain, skull and jaws) and epithelia of the body. We focus on the roles played by key conserved transcription factors Grhl3 and PLAG1 in regulating organ formation and behaviour in vertebrates. Our group also aims to identify supplements that may overcome the severity and/or incidence of birth defects due to genetic deficiency.

Novel genetic pathways in skull, jaw and epithelial formation

Congenital anomalies affecting the formation of the head, skull and jaws (craniofacial defects), are mainly caused by genetic mutations. We focus on the Grainyhead like (Grhl) genes, a key family that regulates craniofacial formation in flies, zebrafish, mice and humans. We developed mouse and zebrafish models with impaired Grhl function, that identify new genetic pathways affecting skull, hard palate and lower jaw formation. Our animal models also identify the role these genes play in establishment and maintenance of healthy epithelia and ensuring correct organ function.

Environmental factors that affect embryonic development

Environmental factors (smoking, alcohol intake and bacterial/viral infection) can cause human birth defects. Supplements (folic acid, magnesium, zinc, vitamin B and iodine) reduce birth defect severity. We use zebrafish embryos and mouse palate explants to identify ways to reduce epithelial and craniofacial defects incidence and severity. We also study the effects of prolonged agricultural organophosphate insecticides exposure on adult behaviour and embryonic development.



Craniofacial skeleton in a zebrafish (Photo credit: Seb Dworkin)

Establishing zebrafish models of human craniofacial defects

Using both germline deletion and transient knockdown approaches, we establish zebrafish lines to model structural human craniofacial skeleton birth defects. By identifying genes that are known to cause birth defects in humans and inhibiting or inactivating the respective zebrafish orthologues of these genes, we study how and why mutations in these genes lead to defects.

Animal models of neurocognitive and behavioural disorders

Using time-lapse microscopy, animal tracking software and mouse and zebrafish behavioural analyses, we study how genetic compromise during embryogenesis can lead to subsequent learning, memory and behavioural issues in later life. Using mouse models deficient for two genes – PLAG1 and Grhl3 - we study the habenula brain region that acts as a "handbrake" to guard against socially-inappropriate or overt risk-taking behaviours. Understanding how this neural center is established and maintained at the genetic level may lead to new therapies.

Lab Head: Assoc Prof Seb Dworkin (s.dworkin@latrobe.edu.au)

Lab members:
Dr Jemma Gasperoni; Mr Jarrad Fuller; Mr Zachary Di Pastena, Ms April Lewis, Ms Maya Salama.

Fields of Study:
Embryology; Genetics; Craniofacial Biology; Neurodevelopment; Animal models of disease.

Capabilities and Techniques:
Zebrafish model system; confocal and fluorescent microscopy; in-situ hybridisation; cartilage & bone staining; PCR & DNA/RNA molecular biology techniques; micro-injection; immunohistochemistry and basic histology; genetically-defined models (mouse, zebrafish) and mouse palate cultures.

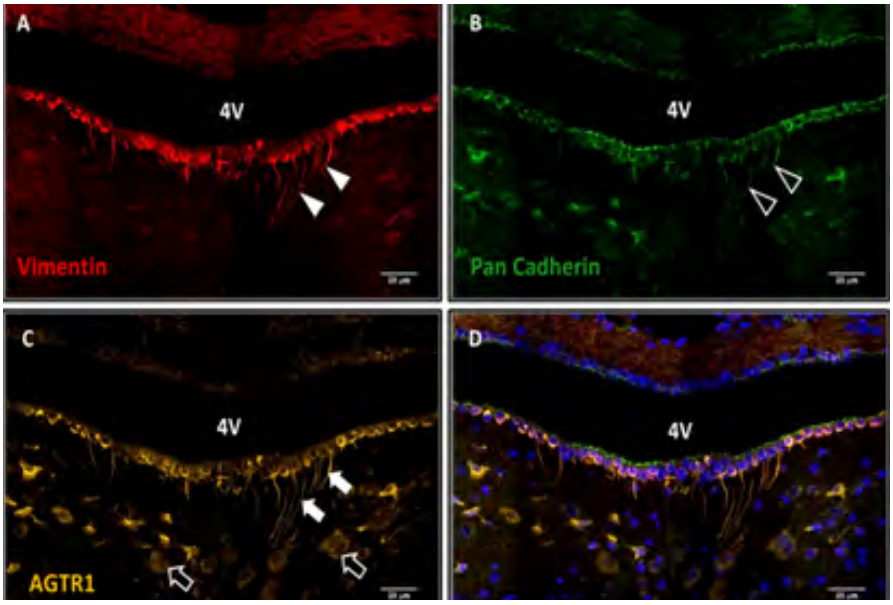
Translational Opportunities:
Genetic counselling; Gene mutation identification for pre- and peri-natal healthcare to ameliorate craniofacial defects and behavioural disorders.

Diabetes Development and Prevention Group

The Diabetes Development and Prevention research group is involved in broad range of research activities which includes experimental, clinical trials and community-based research. The primary aim of our group is to explore risk factors which increases the incidence of diabetes and identifies measures that can be undertaken to prevent the development of this disease and thereby reducing the development of cardiovascular complications. The group uses innovative high-performance clinical and analytical techniques to assess the levels & activity of enzymes, hormones and trace elements in various biological samples in both animal model and human model. The research group has established collaborations with local, national, and international research teams aiming for better prevention and early management of diabetes mellitus and related co-morbidities. The group is also investigating barriers pertaining to diabetes management and wellbeing in people from Culturally And Linguistically Diverse (CALD) communities living with type 2 diabetes Australia. The lab has three main research foci:

The antioxidant, anti-inflammation and hypoglycaemic effects of selected nutraceutical supplements
This research project aims to investigate the effects of a series of nutraceutical supplements (including citrus bioflavonoids and phytosterols) on the levels of oxidative stress, inflammation and glycaemic index in prediabetes and type 2 diabetes mellitus. This project involves research collaboration from local (Professor Grant Drummond, Associate Professor Colleen Thomas, Dr Maria Jelinic), national (Dr Glenn Jacobson – University of Tasmania, Professor Catherine Itsiopoulos – Murdoch University) and international (Dr Lynne Chepulis – Waikato University, NZ).

Indicators of poor glycaemic control
This project aims to highlight the interplay of several biochemical markers associated with poor diabetes outcome which may precipitate the development of diabetes complications including cardiovascular disease. In collaboration with research staff from Charles Sturt University and Khalifa University, UAE, the research team introduced the oxidative stress and inflammation assessment as a routine clinical test of diabetes screening program in rural areas.



Immunofluorescence labeling of vimentin (A), pan cadherin (B), AGTR1 (C) and combined (D) in coronal sections of rat brain (Photo credit: Hayder Al-Aubaidy)

Improve diabetes management in developing countries
This research project focuses on improving the current measures used in early detection and management of type 2 diabetes in developing countries. It has established collaboration with several clinicians and medical researchers from international universities in both Iraq and India to look for better ways to increase awareness of the risks of diabetes and its complications, through early diagnosis of prediabetes and type 2 diabetes mellitus. These research project involves – Dr Jency Thomas, Dr Sabrina Gupta (Local), Dr Ramesh M (JSS university, India), Associate Professor Amani Alhazmi (King Khalid University, Saudi Arabia) & Dr Clarice Tang (Victoria University, Australia).

Lab Head:
Assoc Prof Hayder Al-Aubaidy (halaubaidy@latrobe.edu.au)
Lab members: Dr Jency Thomas; Dr Sabrina Gupta; Dr Dina Jamil; Ms. Deniz Heydarian; Mr Rahul Puvvada; Mr Anwar Althubyani; Ms. Chandana Deekshith; Mr Abdulsatar Jamal; Mr Jad El-Rassi.

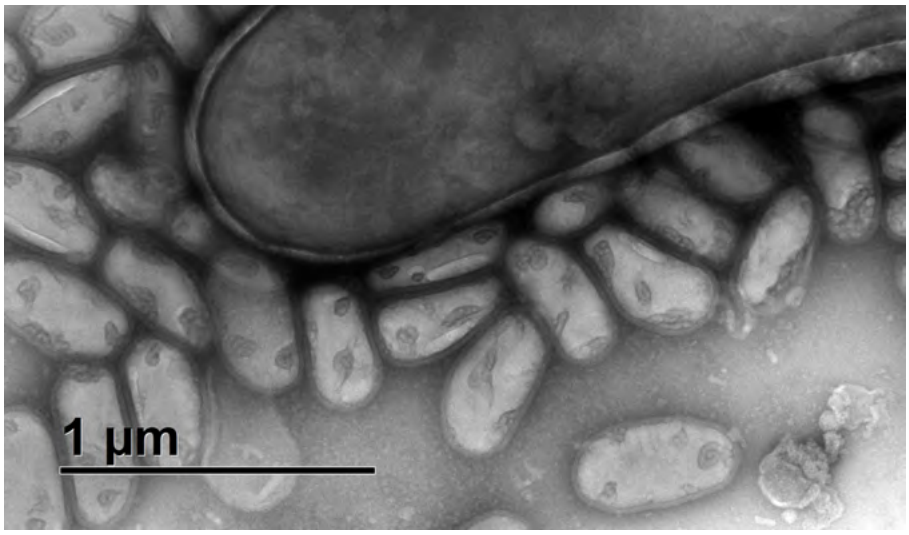
Fields of Study:
Diabetes Mellitus; Cardiovascular Disease Prevention, Diagnosis and Early Management; Nutrition; Public Health; Clinical Sciences.

Capabilities and Techniques:
Ultra-Performance Liquid Chromatography-Mass Spectrophotometry; Enzyme Linked Immunosorbent Assay; Fluorometry; Molecular Biology; Epigenetics; Immunohistochemistry, Semi-structured interviews, Qualitative and Quantitative data analysis.

Translational Opportunities:
Ultra-Performance Liquid Chromatography-Mass Spectrophotometry, Enzyme Linked Immunosorbent Assay, Fluorometry, Molecular Biology and Epigenetics. Quantitative and Qualitative research methodologies, Semi structured interviews, Randomised Control Trials (RCTs) & Community engagement.

Environmental Microbial Genetics Group

We study horizontal gene transfer (HGT), which is the mechanism of gene-swapping between bacteria of unrelated species. HGT provides opportunities for bacterial evolution over long and short timespans. HGT has contributed to antimicrobial-resistance amongst diverse, clinically significant, bacterial species, a situation that now threatens the usefulness of antimicrobials in the treatment of bacterial infections. We study plasmids, transposons and bacteriophages which are vital components of HGT. Our research group uses molecular genetic techniques, transmission electron microscopy, next generation sequencing, microbiological techniques and CRISPR/cas9 gene editing. We also have state of the art equipment, e.g. Illumina MiSeq, Nanopore sequencing facility, bioprocessing fermenter and other equipment to perform genetic analysis.



Transmission Electron Microscope Image of Patescibacterium *Mycolasynbacter amalyticus* infecting *Gordonia pseudoamarae* (Photo credit: Steve Petrovski)

Bacterial horizontal gene transfer in *Pseudomonas aeruginosa*

Bacteria are evolving and are becoming resistant to antibiotics. Understanding how bacteria gain resistance can enable us to control the spread of resistance. *Pseudomonas aeruginosa* is a bacterium that thrives in environments including in humans where it can be part of the normal flora or an opportunistic pathogen that causes serious infections. *Pseudomonas* infection treatment is challenging because it is naturally resistant to antimicrobial agents and can carry plasmids that confer antibiotic resistance. We focus on the genetic elements in *P.* aeruginosa that contribute to the spread of antimicrobial resistance, particularly broad-host-range plasmids which are transmissible between diverse types of Gram-negative bacteria and serve as vehicles for HGT. We study the distribution and evolutionary relationships of these elements as well as the mechanistic basis of their mobility. Our aim is to prevent or limit the spread of antibiotic resistance and our research could also lead to new molecular biology tools that genetically manipulate bacteria.

Population dynamics and biocontrol of wastewater foams

Activated sludge processes remove excess nutrients from wastewater prior to release into other water bodies (oceans and/or lakes) but often fail due to microbiological foams. The brown scum surface foam in aeration tanks contains Candididatus '*Microthrix parvicella*' or "Mycolata" bacteria. We apply lytic bacteriophages directly to activated sludge plants to reduce the bacterial cell numbers below the foaming threshold. We have isolated >100 mycolata bacteriophages and have shown that we are able to reduce their growth. We also study bacteriophage interactions to identify their population dynamics.

Patescibacteria, or Candidate Phyla Radiation, are diverse bacteria mostly uncultivated and known as microbial dark matter. Our lab has developed a method to isolate and culture these ultrasmall microbes from wastewater treatment plants. They have reduced genomes and parasitise hots bacteria I.e. *Gordonia amarae.* The mechanism of their growth and cell cycle are largely unknown. We are investigating their lifecylces to understand Patescibacteria's unique biology and aim to control problematic bacterial growth in wastewater treatment plants by manipulating their growth.

Lab Head: Assoc Prof Steve Petrovski (steve.petrovski@latrobe.edu.au)

Lab members:
Dr Mark Chan; Mr Jayson Rose;
Ms Liana Theodoridis; Ms Mikaela Whitty;
Ms Jessica Owen, Mr Jed Chafer;
Ms Caroline Xavier; Ms Laura Viola.

Fields of Study:
Microbiology; Genetics; Microbial Ecology; Evolution; Biosensors.

Capabilities and Techniques:
Electron microscopy; Next Generation Sequencing; Microbial assays; Molecular Biology.

Translational Opportunities:
Developing potential bacteriophage cocktails to be applied to wastewater treatment plants to control bacterial proliferation that cause foaming and bulking; Developing novel pharmaceutical products containing bacteriophages; Developing Phage biosensors detection tools for use by Australian Defence Force.

Healthy Brain Ageing & Dementia Research Group

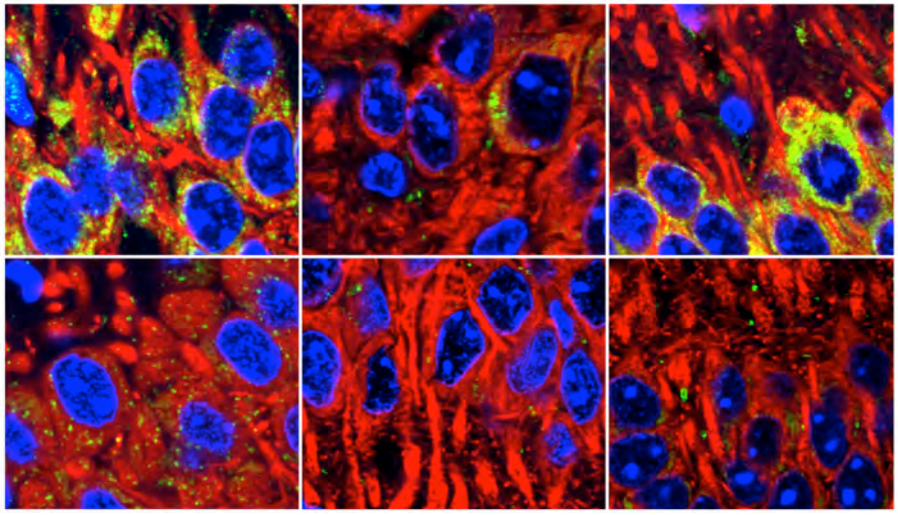
Our group aims to identify the epigenetic and molecular mechanisms involved in the injury process of vascular dementia (VaD) in order to develop new therapies for its treatment. Through our research, we have discovered many potential targets and have utilized a range of pharmacological agents.

The Hypoxisome in Neuronal Resilience and Cell Death

Our research has uncovered that both hypoxia, which occurs due to oxygen deprivation at the tissue level, and cerebral ischaemia, which results from insufficient blood flow to the brain, activate five signalling pathways that converge on the hypoxisome - a nuclear multi-protein complex that is associated with DNA. The hypoxisome controls genes that dictate the fate of neurons. Our primary focus is toinvestigate the effect of hypoxisome on cell death following ischaemic stroke, specifically in cases of severe injury where the hypoxisome up-regulates proteins that trigger and execute neuronal death programs. Additionally, we are studying the hypoxisome during the post-stroke remodelling phase, where it up-regulates adaptive stress response genes encoding proteins that promote neuronal survival. By understanding the role of the hypoxisome in both detrimental and beneficial post-stroke processes, our research aims to develop new therapeutic strategies for treating ischaemic stroke.

Uncovering the Mechanisms of Sterile Neuroinflammation in Stroke and Vascular Dementia (VaD)

Neuroinflammation is known to cause neuronal tissue damage, impairments, and disabilities. However, the mechanisms that initiate neuroinflammation in vascular dementia (VaD) remain poorly understood. Our research has revealed that cerebral hypoperfusion activates innate immune receptors, which then trigger signalling cascades that activate protein kinases, leading to an inflammatory response. This activation of intracellular signalling pathways results in an increased production of inflammasomes, which are multi-protein complexes that contribute to tissue injury and cell death. In our animal model of VaD, we have observed that inflammasomes play a critical role in neuronal tissue damage and behaviour. Specifically, we are investigating how immune receptors recognize self-ligands in neurons undergoing metabolic stress, and activate inflammasomes and caspase-1, ultimately leading to neuronal injury or death. Additionally, our research focuses on how blocking the inflammasome signalling pathways weakens the initiation and amplification of inflammatory cell responses, thereby improving functional outcomes. Our findings provide a novel avenue for the development of potential therapeutic targets for the treatment of VaD .



Immunofluorescence images of inflammasome activation in the hippocampus in Vascular Dementia (Photo credit: Garrie Arumugam)

Intermittent Metabolic Switching and Epigenetics

Recent studies have revealed that individuals with metabolic diseases have an elevated risk for age-related neurological disorders. Intermittent fasting, a dietary protocol characterised by alternating periods of feeding and fasting, has been shown to mitigate or prevent cellular dysfunction and degeneration in various cardiovascular disease models, including dementia. However, the precise mechanisms by which intermittent fasting modifies the expression of proteins involved in these protective effects remain to be elucidated. Our research demonstrates that intermittent fasting provides protection against both ischaemic stroke and VaD. Previous investigations have shown that epigenetic germline inheritance of diet can lead to obesity and insulin resistance. In our own work, we have observed epigenetic changes in animals following intermittent fasting, which may underlie the beneficial effects seen in a range of disease conditions. We seek to identify specific intermittent fasting-induced epigenetic changes that promote expression of protective genes and ultimately improve outcomes in ischaemic stroke and vascular dementia.

Lab Head: Prof Thiruma V. Arumugam (Garrie) (g.arumugam@latrobe.edu.au)
Lab members: Dr Irene Cheng; Dr Vernise Lim; Dr Vanessa Johanssen; Ms Nishat Tabassum; Mr Yibo Fan; Mr Xiangyuan Peng; Mr Xiangru Cheng; Ms Aayushi Arora; Mr Marconi Fung; Ms Jyotsnna Ranjithkumar.

Fields of Study:
Neurobiology; Pharmacology; Molecular Biology; Epigenetics; Neurodegeneration; Ageing.

Capabilities and Techniques:
Ischaemic stroke and vascular dementia animal models; Molecular Biology; RNA sequencing; Genomics; Proteomics; Flow Cytometry; Bioimaging; Cognitive Testing.

Translational Opportunities:
Our research on the hypoxisome and inflammasome has revealed novel mechanisms of cell death and potential therapeutic targets for ischaemic stroke and vascular dementia. Our findings hold promise for clinical translation and have already played an instrumental role in initiating three clinical trials for stroke treatment.

Hypertension and Diabetes Research Group

Cardiometabolic disease claims 40,000 Australian lives per year due to events such as heart attack and stroke. While current medications, which include blood pressure- and cholesterol-lowering agents, reduce the risk of a deadly event in some patients, they are not effective in all cases. Many patients remain at risk of a heart attack or stroke despite receiving best available care. Clearly, there are disease mechanisms at play that current medicines don't address. Our group is focused on identifying what these unknown mechanisms are and using the knowledge to identify new biomarkers for early disease detection and to develop more effective therapies. We use animal and cell culture models of cardiometabolic disease, as well as physiology, immunology, molecular biology, genomic and imaging techniques.

The NLRP3 Inflammasome and hypertensive end-organ disease

Hypertension (high blood pressure) affects 40% of adults and is the leading risk factor for heart disease and stroke. It also promotes kidney disease, dementia and retinopathy (vision impairment). Drugs that increase urine production, dilate blood vessels and/or reduce heart rate are used to reduce blood pressure; but, over half of all patients still cannot control their blood pressure with these medications. Hypertension also affects the immune system. We discovered that an immune complex called the NLRP3 inflammasome, contributes to the development of hypertension. Knocking out the genes that code for the NLRP3 inflammasome, or its cytokine product interleukin-18 (IL-18), reduces blood pressure, kidney injury and heart failure in mice with hypertension. Our current focus is on developing and screening novel drugs that block IL-18 or its receptor and determining their effectiveness at treating hypertension and its downstream consequences of kidney disease and heart failure

Deciphering the gut phageome and its role in hypertension

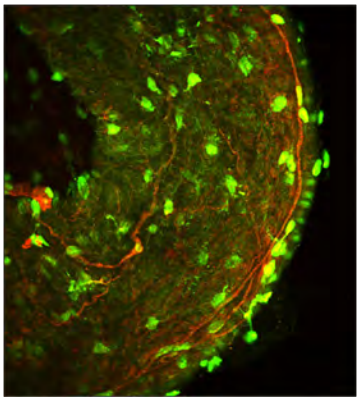
An imbalance in the gut bacterial communities can contribute to hypertension and related end-organ damage. However, an understudied yet vital organism in the gut are phages - viruses that infect and kill bacteria. We have discovered several phages that are highly abundant during experimental hypertension that are known to kill the 'good' bacteria of the gut. These phages may be prime targets for new treatments to improve gut health and high blood pressure.

Understanding the cellular and molecular drivers of heart attacks

Heart attacks are a major cause of global death and disability. They occur when the coronary arteries – which supply blood to the heart – become blocked by fatty deposits called atherosclerotic plaques. Early detection and therapies that slow or halt their development could prevent blockages. This project will comprehensively explore human atherosclerosis biology using powerful multiomic approaches that include single-nucleus RNA sequencing, spatial transcriptomics, and imaging mass cytometry (through collaborations with the University of Sydney) tools to human coronary artery specimens. This study will likely identify: (1) candidate biomarkers for early detection of atherosclerotic plaques; and (2) crucial disease pathways that could serve as targets for future therapies to halt/ reverse atherosclerotic plaque development.

Comparing the effects of intermittent fasting and sex in metabolic syndrome

Intermittent fasting is an effective and natural strategy for weight control. It can also reverse metabolic disturbances such as hyperglycemia, hypertension, and unhealthy levels of fat in the bloodstream. Many studies have shown the beneficial effects of intermittent fasting in the setting of metabolic syndrome, but very few studies have considered the effect of sex, which our work will now investigate..



Inflammatory macrophages (green) accumulating in blood vessels from a pre-clinical model of high blood pressure

Lab Heads:
Assoc Prof Antony Vinh
(a.vinh@latrobe.edu.au) and
Dr Maria Jelinic (m.jelinic@latrobe.edu.au)

Lab members:
Dr Courtney Judkins; Dr Hericka Bruna Figueiredo Galvao; Dr Vivian Tran; Ms Flavia Wassef; Ms Buddhila Wickramasinghe; Ms Tayla Gibson Hughes; Mr Jake Robertson; Ms Ghaida Moria; Mr Roberto Iaconis; Mr Patrick Francis; Mr Vinh Nguyen Son Ngo.

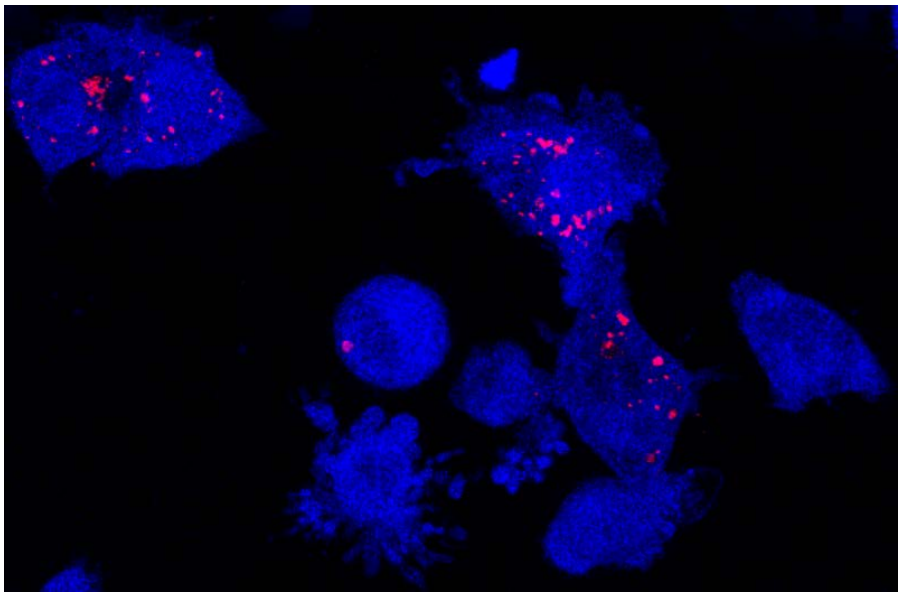
Fields of Study:
Hypertension; Diabetes; Obesity; Immunology; Pharmacology

Capabilities and Techniques:
Animal models of hypertension, diabetes and obesity; flow cytometry; histopathology; immunohistochemistry; biomedical imaging; confocal microscopy; genomic sequencing; spatial transcriptomics; in vivo cardiovascular/renal function; oxidative stress & inflammation assessment; vascular reactivity/compliance.

Translational Opportunities:
Drug discovery, validation; pre-clinical chronic kidney/liver/vascular disease drug assessment; hypertension/diabetes therapy and dietary interventions.v cdf

Inflammasomes and Innate Immunity Group

Inflammation is the body's defense against injury or infection, but when it becomes excessive or prolonged, it can lead to diseases like autoimmune disorders and chronic conditions. The innate immune system, our first line of defense, triggers inflammation to fight pathogens and heal tissues. Inflammasomes, protein complexes in immune cells, detect harmful stimuli and activate inflammation to protect and repair the body. However, excessive or chronic activation of Toll-like receptors (TLRs) and Inflammasomes can lead to diseases such as neurodegenerative, pulmonary, metabolic, and gastrointestinal diseases, even cancer. Our research focuses on how the innate immune system recognises pathogens, activates immune sensors like Toll-like receptors and inflammasomes, and aims to develop therapies to reduce harmful inflammation and provide relief to patients



Inflammasome activation in macrophages challenged by viral aggregates (red). (Photo credit: Ashley Mansell)

Inflammasomes and mucosal immunology
Inflammasomes are crucial in the immune response to bacterial and viral infections. Our group has identified their role in infectious diseases and the benefits of targeting inflammasomes to reduce inflammation in pathogen-related diseases. In collaboration with researchers at the Hudson Institute and UNSW, we are studying inflammasomes in acute and chronic inflammatory diseases using human patient stem cell-derived organoids. We aim to assess the therapeutic potential of NLRP-targeted treatments. These studies will explore inflammasome activation in the pulmonary and intestinal mucosal barriers during chronic inflammation and pathogen-related diseases. Further research will evaluate the effectiveness of targeting inflammasomes to treat these conditions. Additionally, in partnership with the Helbig lab, we are examining the role of inflammasomes in viral infections like Dengue and Zika, and their potential as therapeutic targets to reduce inflammation. Drawing on our previous identification of viral aggregate proteins as a novel class of inflammasome activators, we are also identifying and characterising new viral aggregates that drive the inflammation associated with these viral infections.

Inflammasome Drug Development
In conjunction with the Dutton group, we are leveraging our previous characterisation of the world's only dual inflammasome inhibitor, to intelligently design and validate new lead drug candidates with improved drug-like properties to treat the inflammation associated with inflammasome-related diseases.

TLR Signal Transduction and Immunometabolism
Immunometabolism describes the interplay between immunological and metabolic processes which are critical to the immediate innate immune response to infection. Dysfunctional metabolism underlies many inflammatory diseases, the identification of key regulators of selective metabolic programs providing the framework for next generation therapeutic agents for function-specific immunometabolic targeting. With colleagues at the Hudson Institute, we identified a role for the critical immune modulator STAT3 in regulating the immunometabolic programming of TLR-activated macrophage mitochondria. Our studies aim to understand the mechanisms of action of mitochondrial STAT3 and regulation of the Electron Transfer Chain and mitochondrial respiration.

Lab Head: Assoc Prof Ashley Mansell (A.Mansell@latrobe.edu.au)
Lab Members: Mr Ethan Reidy; Mr Kye Vahland; Mr Cameron McDonald.

Fields of Study:
Innate Immunology, Inflammation, Drug Development, Infectious Diseases, Mucosal Immunology.

Capabilities and Techniques:
In vivo and *in vitro* models of disease, microscopy, live-cell imaging, inflammation screening, drug screening, cell biology.

Translational Opportunities:
Inflammasome and TLR drug screening platform, drug development, pre-clinical disease models

Molecular Cell Biology Laboratory

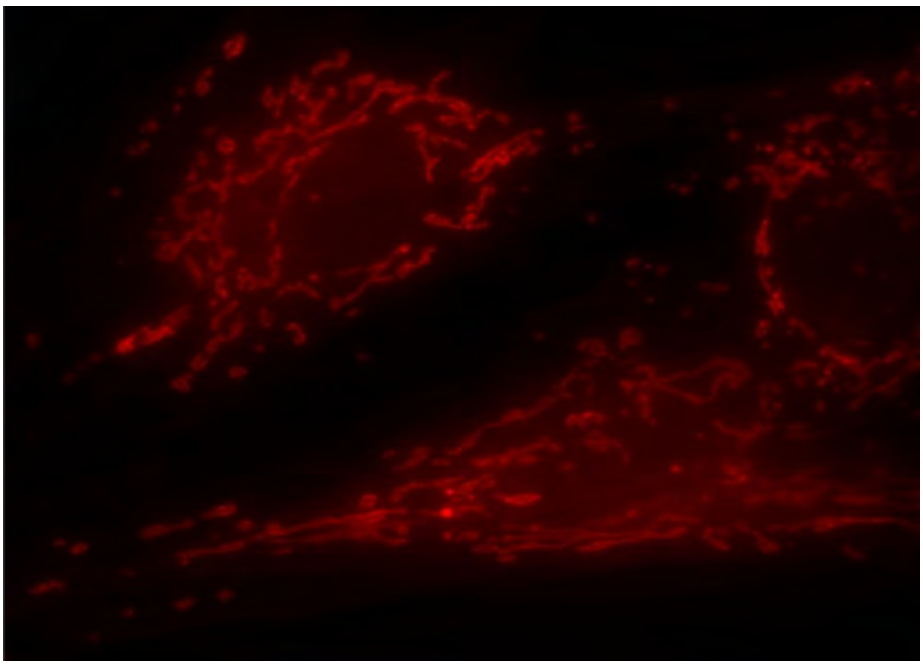
My laboratory investigates diseases that affect the central nervous system and collectively represent a significant proportion of the burden of disease in adults worldwide. I focus on three main disorders, Parkinson's Disease, Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome (ME/CFS) and Long COVID. My laboratory aims to characterise these disorders, investigating the mechanisms of the disease process at the cellular and molecular level. We aim to discover how these mechanisms can be manipulated for treatment and to identify biomarkers which can be developed into world-first diagnostic tests.

Parkinson's Disease

Parkinson's Disease (PD), is the second most common neurodegenerative disorder worldwide. Most cases of PD are sporadic with no known genetic cause but a small percentage of patients (5-10%) are due to inherited genetic mutations. We use blood cells from patients with sporadic and genetic forms of PD. Our main objectives are to increase our understanding of the underlying disease mechanisms and pathways, identify biomarkers of the disease, identify patients early in the disease process prior to clinical diagnosis and test the effectiveness of various substances. We do this via analysing mitochondrial and lysosomal function, activity levels of proteins, measurement of calcium responses and analysis of gene expression changes.

Myalgic Encephalitis/Chronic Fatigue Syndrome (ME/CFS)

ME/CFS is a debilitating chronic condition characterised by a disabling fatigue and a post-exertional malaise which is a worsening of symptoms after a mental or physical exertion. The disease is triggered by a range of bodily insults, most commonly a viral infection. Currently there is no cure and no clear treatments or diagnostic tests are available. My laboratory is working to unravel the underlying disease mechanisms with a focus on immunometabolism, gut microbiota and immune function.



Fibroblast mito. (Photo Credit: Sarah Annesley)

By understanding the underlying disease mechanisms we aim to develop viable treatment options. We have also identified biomarkers of the disease and are working towards validating these biomarkers in larger and more varied cohorts with the ultimate aim of developing a much needed diagnostic test.

Long Covid

Beyond the immediate acute effects of the virus responsible for the COVID-19 pandemic a large number of people are experiencing ongoing symptoms many weeks and months beyond the original infection. The illness afflicting these patients is termed Long COVID and it shares many similarities with ME/CFS. My laboratory has i dentified biomarkers of Long COVID and are working with a large team of researchers to further validate these in a large cohort. This work aims to develop a multibiomarker panel which will have high diagnostic potential. My laboratory is also investigating the underlying disease mechanisms and the overlap with ME/CFS.

Lab Head: Dr Sarah Annesley (s.annesley@latrobe.edu.au)

Lab Members:
Dr. Daniel Missailidis; Ms Oana Sanislav; Dr. Claire Allan; Mr Benjamin Arnold; Ms Tina Katsaros; Mr Eric Okrah; Ms Zoe Whitehouse; Ms Kayla Kurt

Fields of Study:
Cell Biology, Metabolism; Molecular Biology; Molecular Genetics.

Capabilities and Techniques:
All techniques of molecular biology; Seahorse respirometry assays; enzyme activity assays; immunofluorescence microscopy; diverse FRET-based; fluorometric and luminometric assays of cellular functions; transcriptomics; proteomics.

Translational Opportunities:
We have identified biomarkers for Long COVID, ME/CFS and Parkinson's Disease and have published these results. We are now working at validating these biomarkers in larger and more varied cohorts. This is the first step in development of world first diagnostic tests for these diseases.

Musculoskeletal Research Group

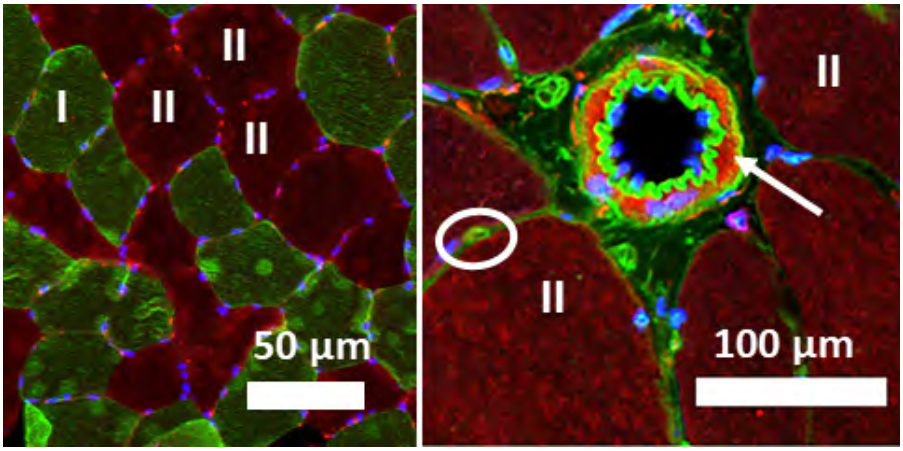
Skeletal muscle tissue (the largest mass in the human body) accounts for 45% of total body weight and is essential for human health adapting in function and metabolism in response to increased physical activity and changes to metabolic demands. Loss of skeletal muscle mass leads to devastating consequences causing permanent disability and mortality in many conditions, including cancer, chronic heart failure, burn injury, kidney disease, diabetes, ageing, disuse, and numerous genetic disorders such as muscular dystrophy. We aim to understand the cellular mechanisms that regulate muscle plasticity and adaptation, so that we can identify new targets or develop treatment options for conditions with compromised skeletal muscle health. We study skeletal muscle adaptation and plasticity via a translational research approach using pre-clinical laboratory models including cell culture and multiple animal models of muscle adaptation and plasticity that are complemented with clinical models of exercise in humans.

Identifying novel supplements for muscle health

Endurance athletes consume supplements to minimize exercise-induced stress and enhance recovery and performance. Many supplements claim to positively influence exercise induced muscle adaptation but are poorly investigated regarding in vivo activity and efficacy in humans. We aim to understand supplement effects on healthy skeletal muscle function.

Improving muscle regeneration

Skeletal muscle sports injuries are frequently associated with significant morbidity and prolonged loss of function. After injury, skeletal muscle regeneration has distinct phases: inflammation, degeneration and regeneration. These phase transitions are not fully understood. We use complementary cell culture experiments and muscle injury and regeneration animal models to study new muscle repair improvement therapies.



Fluorescent staining of myosin heavy chain and blood vessel in skeletal muscle (Photo credit: Nicole Stupka)

Characterizing genetic models of myopathy

Effective treatments for myopathies are difficult to find because the molecular changes underlying clinical phenotypes are poorly understood. Few mammalian models are available to study disease progression from juveniles to adult and finally in elderly mammals. Ageing effects are important for muscle related disorders as age-related changes in normal muscle protein expression, muscle strength and fibre-type composition can impact animal model responses to therapeutic strategies and pre-clinical therapeutic drug testing. We characterize and define age related changes in skeletal muscle phenotype in new muscle pathology models. We characterize new RyR1 myopathy models to test therapeutic strategies and drugs.

Lab Head:
Dr Chris van der Poel
(c.vanderpoel@latrobe.edu.au)

Lab Members:
Dr Travis Dutka; Dr Andy Govus; Dr Brett Gordon.

Fields of Study:
Skeletal Muscle; Sports Medicine; Cell Physiology.

Capabilities and Techniques:
Muscle injury models (chemical, stretch, and ischaemia-reperfusion); Skeletal muscle contractile function testing (in vitro, in situ); histology; immunohistochemistry; cell culture; biochemistry.

Translational Opportunities:
Muscle strength; Inflammatory Myopathies; Genetic Myopathies; Sarcopenia; Sports Supplements; Skeletal muscle health; Adaptation to exercise.

Pain and Childbirth Group

There is an urgent need to improve approaches to supporting women through childbirth, to promote normal birth and positive experiences for women.

The pain associated with labour is unique and complex. While typical occurrences of pain tend to be associated with injury or disease, labour pain is different. It arises during a natural process in which it plays a role in driving the hormonal events of labour.

Despite the unique context and function of labour pain – which differentiates it from the pain associated with injury or disease – labour pain is most commonly treated as a pathological pain, associated with suffering. Rates of birth trauma, fear of birth and medical intervention during childbirth are escalating in developed countries, leading to increased exposure to risks and poorer health outcomes for women and babies. Compounding the issue, women exposed to high intervention rates who also perceive intrapartum care to be poor, are more likely to experience acute trauma symptoms.

Dr Laura Whitburn leads an innovative research program to better understand the experience of childbirth based on contemporary pain science and consciousness theories. This work looks at the neurobiological mechanisms behind childbirth and how these influence women's conscious state and perceptions during labour. This includes the role of the nocebo effect, where negative experiences can be elicited through verbal and non-verbal cues.

This aim of this program is to enhance the care provided to women during this transformative event, to improve the health of mothers and their babies and reduce rates of birth trauma.

Persephone's Birth (Photo credit: Jason Lander)

Current projects:

- Labour pain assessment: Evaluating a new woman-centred approach
- The language of labour pain: Understanding how words influence women's experiences of labour pain
- Midwives' views and experiences of supporting women to manage labour pain

Lab Head: Dr Laura Whitburn (l.whitburn@latrob.edu.au)

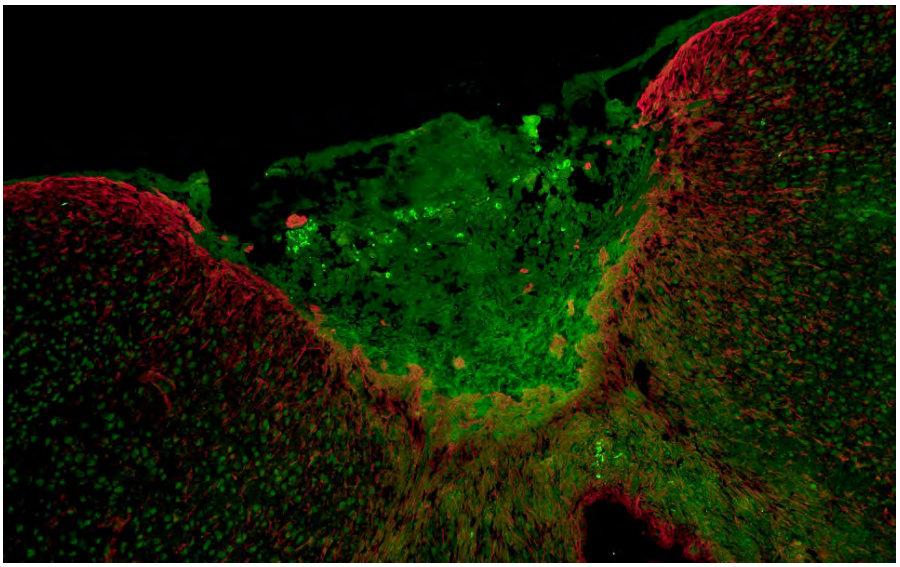
Fields of Study:
Medical and Health Sciences; Midwifery; Physiotherapy; Obstetrics; Gynaecology.

Capabilities and Techniques:
Qualitative research methods, particularly phenomenology; Longitudinal cohort studies.

Translational Opportunities:
The outcomes of this research aim to influence current practices in supporting women in labour, including policy and models of care.

Stroke and Brain Inflammation Group

Our research group aims to understand the fundamental injury and repair mechanisms which occur during stroke. A stroke triggers a series of damaging events following its onset, including inflammation and systemic infection that lead to cell death and changes in mobility. Our team has introduced routine immunological approaches that are now widely used in this field to tackle inflammation. Our key research focuses on whether immunotherapies – that is therapies which either suppress or activate the body's immune response - can be used to reduce brain inflammation and consequently reduce the burden of stroke. The team has extensive expertise using rodent studies, as well as new approaches to analysing large data sets to identify new relationships in stroke pathology. Our team aims to address gaps in existing research by addressing key risk factors such as advanced age and sex in our work.



Immunofluorescence image of glial scar surrounding the infarct area after stroke (Photo credit: Samoda Rupasinghe)

Targeting inflammation in stroke

Stroke, from insufficient blood flow to the brain, is treated by clot-buster drugs or surgical clot removal to restore blood flow. However, these interventions are only suitable for 20% of patients and must be used quickly requiring advanced neuroimaging facilities. Brain cells may rapidly die from lack of oxygen or later from inflammation. We study acute and chronic stroke treatments that target and neutralise local inflammation. We assess brain injury, inflammation, motor function and cognition impairment in animal models of stroke, and examine immunotherapies as a treatment for stroke.

Amniotic cell therapy in stroke

We have found that treatment with human amnion epithelial cells (hAECs) is neuroprotective when administered within the acute phase of experimental stroke. That work has been translated into a Phase I clinical trial of hAECs in 8 acute stroke patients. We are also identifying how long after a stroke that hAEC therapy might still be beneficial. We routinely incorporate aged mice of both sexes into our preclinical studies to better simulate the clinical scenario.

hAEC-derived extracellular vesicles in stroke

We are extending our work on hAECs by exploring the potential of tiny particles (extracellular vesicles) released by the cells as another attractive stroke therapy. Extracellular vesicles (40-120 nm in size) can act as signalling mediators between cells, and those released by hAECs contain material that supports blood vessel development and tissue healing. We predict that extracellular vesicles from hAECs may be protective after stroke when simply administered intravenously or intranasally. Purified extracellular vesicles are more drug-like than hAECs and can be readily stored and quickly prepared for use.

Estrogen receptor signalling in stroke

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. We have previously found that drugs selectively targeting a novel estrogen receptor (GPER1) can substantially influence stroke outcome in a sex-dependent manner. Using mice deficient in GPER1, our research aims to gain a better understanding of sex difference in outcome after stroke, in terms of brain injury and inflammation. Furthermore, we aim to elucidate the importance of GPER1 of estrogen signalling using a selective antagonist, G-15, and agonist, Tamoxifen.

Lab Head: Dr Helena Kim (h.kim2@latrobe.edu.au)
Lab members: Dr Richard Zhang; Mr Satar Jamal; Mr Tymon van Diemen.

Fields of Study:
Stroke; Brain inflammation; Neuroprotection; Cell therapy; Immunotherapy.

Capabilities and Techniques:
Ischemic stroke animal models; Animal behavioural testing; Immunofluorescence; Flow cytometry; Molecular biology; RNA sequencing; Genomics; Big data analysis.

Translational Opportunities:
Our findings hold promise for clinical translation and have already played an instrumental role in initiating three clinical trials for stroke treatment.

The Bay Group - Microbial Ecology, Biogeochemistry & Global Change

Mission
We advance research on the microbial ecology of terrestrial and aquatic ecosystems, tackling global challenges including environmental degradation, food security, and climate change. We mentor future leaders and scientists in an inclusive and collaborative setting that fosters innovation and a deeper understanding of complex systems.

Biodiversity, Function & Activity
Microbes thrive in diverse and extreme habitats like deserts, salt lakes, caves, and the deep ocean, defying the notion that these environments are too extreme for life to persist. Our research reveals that many bacteria are metabolically flexible, capable of dormancy, and can utilize various organic and inorganic energy sources, including atmospheric trace gases, to survive and grow. Studying these microbes and their diversity, ecology, and function enhances our understanding of how life persists, and biodiversity is maintained in the face of climate risks such as desertification and nutrient depletion.

Soil Fertility & Environmental Resilience
Soil biomes are complex ecosystems rich in microbial diversity, which play a crucial role in soil productivity. These microbes facilitate nutrient cycling, decompose organic material, and support plant health. By studying the structural and functional aspects of microbial biodiversity in soils, we can gain insights into their contribution to ecosystem services. This understanding can inform strategies to improve soil health, resilience to disturbance and enhance productivity, contributing to sustainable agricultural and environmental practices.

Atmospheric Change & Global Cycles
Microorganisms are essential in driving global biogeochemical cycles, encompassing carbon and various nutrient cycles. They regulate greenhouse gases like methane, carbon dioxide, and nitrous oxide, which are vital for climate regulation. Our research indicates that soil bacteria are instrumental in cycling these gases through a range of ecosystems. Understanding these microbial processes across different ecosystems and land use types is critical for devising effective climate change mitigation strategies.

Impact
Our research provides fundamental insights into the biogeochemistry of environmental microbiota. This provides a basis for to enhance environmental stability, food security and mitigate climate change.

Lab Head:
Dr Sean K. Bay (s.bay@latrobe.edu.au)

Lab Members:
M. Nayeli Luis-Vargas (PhD candidate),
Alyza Lynch (MSc Candidate),
Phil Bottomly (B.Hons. Candidate).

Fields of Study:
Environmental Microbiology; Computational Biology; Biogeochemistry;
Microbial Ecology.

Capabilities and Techniques: Bioinformatics, Multi-omics, Gas chromatography, Microbial activity studies, Isotope studies, Nutrient budgets, Soil physicochemistry, GIS.

Translational Opportunities:
Microbial biodiversity of soil and aquatic systems, Atmospheric gas, carbon and nutrient budgets. Monitoring soil fertility and environmental degradation.

Contact:
If you are interested in joining us, collaboration or learning more about our research, please contact us directly on:
E - s.bay@latrobe.edu.au
P – 03 9479 1501

About La Trobe University

Our Mission

Advancing knowledge and learning to shape the future of our students and communities.

Our Vision

To promote positive change and address the major issues of our time through being connected, inclusive and excellent.

Our Values

Our early reputation as a radical and challenging institution continues to in uence the way we enrich the experience of our students and engage with our partners and communities.

We were founded half a century ago to broaden participation in higher education in Melbourne's north and, later, in regional Victoria. We have succeeded for many thousands of students who would otherwise have been excluded from the opportunities provided by a university education.

We continue to support access, diversity and inclusivity while undertaking world-class research that aims to address the global forces shaping our world and make a difference to some of the world's most pressing problems, including climate change, securing food, water and the environment, building healthy communities, and creating a more just and sustainable future.This approach is based on our values of:

- inclusiveness, diversity, equity and social justice
- pursuing excellence and sustainability in everything we do
- championing our local communities in Melbourne's north and regional Victoria
- being willing to innovate and disrupt the traditional way of doing things.

Of all Australian universities, we are the most successful at combining accessibility and excellence, and have become a place where social inclusion and globally-recognised excellence come together for the bene t of our students, our staff and our communities.

Our academics and researchers achieve national and international recognition, our public intellectuals demonstrate an enduring social conscience and in uence, and our alumni achieve extraordinary success and impact in government, industry and not for pro t organisations.

We strive to be exemplars for the sector in our commitment to gender equity and to inclusivity for marginalised groups; and we work with indigenous peoples and organisations to support their social, cultural and economic aspirations.

We embrace sustainable practices across all our campuses because we are committed to improving environmental, social and economic outcomes for our communities.

We contribute to economic development for our local communities, and our future activity will increasingly be international as we become a globally connected university in everything we do.

Our Culture

La Trobe Cultural Qualities

Our cultural qualities underpin everything we do. As we work towards realising the strategic goals of the University we strive to work in a way which is aligned to our four cultural qualities:

Connected

- We are Connected: Connecting the students and communities we serve to the world outside

Innovative

- We are Innovative: Tackling the big issues of our time to transform the lives of our students and society

Accountable

- We are Accountable: Striving for excellence in everything we do. Holding each other to account, and working the highest standards

Care

- We Care: We care about what we do and why we do it, because we believe in the power of education and research to transform lives and global society.

About Victoria and Melbourne

Experience Melbourne

Melbourne is the capital of the state of Victoria, and Australia's second largest city. It's a multicultural hub with 4.5 million people from over 153 countries. It's one of the world's best sporting cities, and is Australia's art and culture capital. Melbourne is a safe, well-serviced city in which to live. The main campus of the University at Bundoora is close to many world class hospitals, schools, research centres, shopping centres, bike paths and parklands. Melbournians enjoy, affordable healthcare, world-class education, reliable infrastructure, business opportunities and a healthy environment. In Melbourne you'll find just about every cuisine: French, Italian, Spanish, Greek, Chinese, Malaysian, Indian, Thai, Japanese, Moroccan and lots more. Melbourne has over 100 art galleries as well as theatres, international and local opera, ballet, comedy and live music.

Each year Melbourne hosts major international sporting events like the Australian Open Grand Slam tennis tournament, the Formula One Grand Prix, the Rip Curl Pro surfing championship, the Australian Masters golf tournament, the Melbourne Cup and the Grand Final of Australian Rules Football. As well as over 2500 festivals and events including the Melbourne International Arts Festival, Melbourne International Film Festival, Melbourne International Comedy Festival and the Melbourne Spring Racing Carnival.

Find out more: https://liveinmelbourne.vic.gov.au/discover

Victoria: The Garden State

Victoria has many notable gardens and 36 national parks covering two and a half million hectares. Victoria's many attractions include the Great Ocean Road, (stunning coastal views and the world-famous Twelve Apostles), the Grampians and the High Country.

Find outmorevisitvictoria.com

La Trobe University Campuses in Australia

Each of our seven campuses (Melbourne, Albury-Wodonga, City, Bendigo, Shepparton, Midura and Sydney) is a unique expression of place, people and history that play an important role in social, cultural and economic life. We are located in Victoria's major regional cities, creating a unique network of research, industry and innovation expertise that can be accessed across the state.

Melbourne Campus

La Trobe's Melbourne Campus has 27,000+ students and is surrounded by bushland. Students from across the world take advantage of state-of-the-art facilities, including our AgriBio Research Centre, the La Trobe Institute for Molecular Science and our very own Wildlife Sanctuary.

Albury-Wodonga Campus

La Trobe's Albury-Wodonga Campus has 800+ students and is home to our leading regional research centre, the Centre for Freshwater Ecosystems which focuses on water science and policy of the Murray-Darling basin. Here, undergraduate students work alongside Honours and research students on local issues.

School of Agriculture,
Biomedicine and Environment
La Trobe University