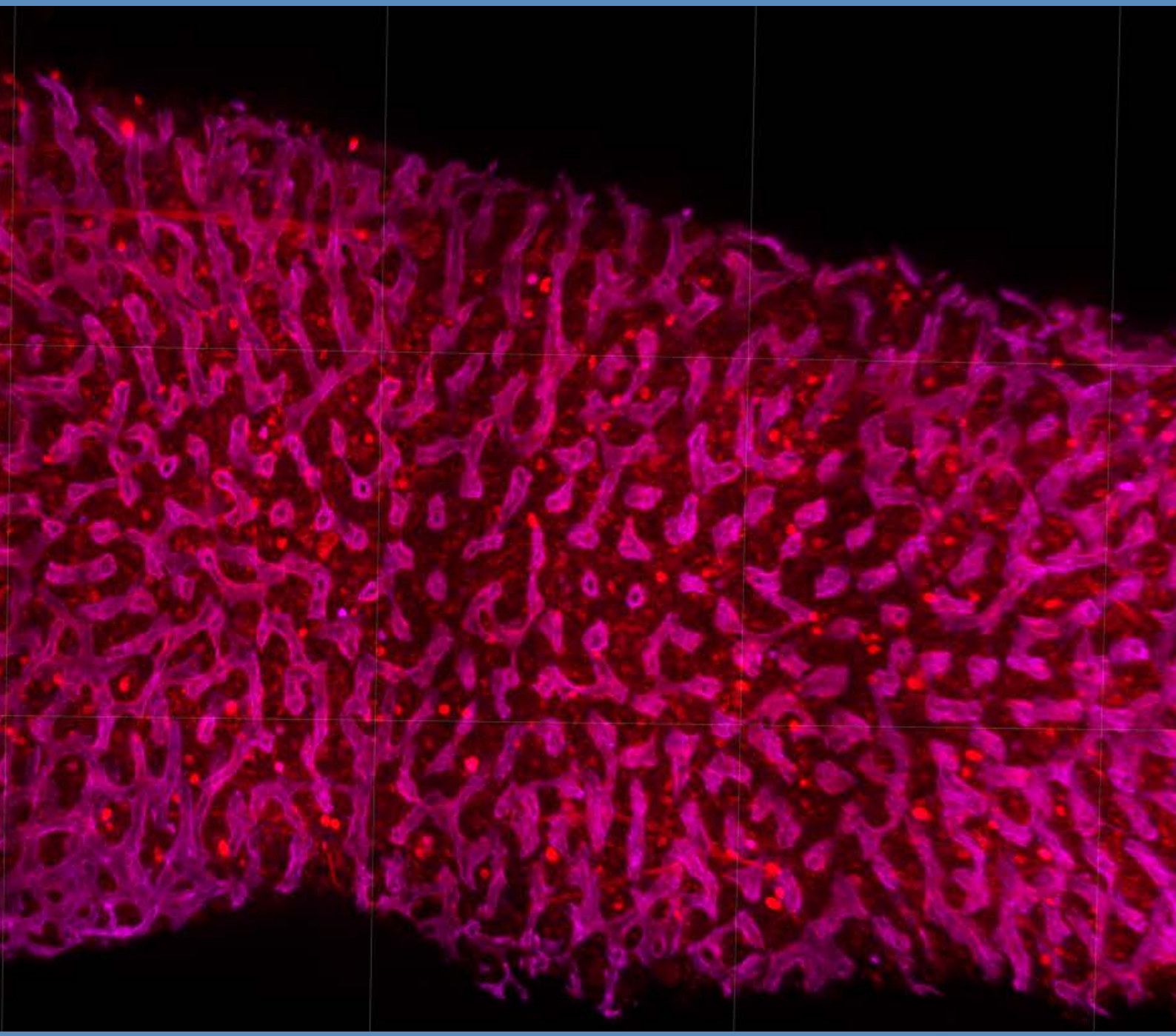
LA TROBE
UNIVERSITY • AUSTRALIA

Baker Department of Cardiovascular Research, Translation and Implementation

School of Agriculture, Biomedicine and Environment

Scientistific experts in cardiovascular disease, diabetes and public health research.
Together, we are translating our discoveries into practice.



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

Contents

Cover Photo:
The vascular network of the bone marrow (Photo Credit: Dr Man Kit Sam Lee)

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:

- 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)
- Research Centre for Future Landscapes (collaboration with the Arthur Rylah Institute of DELWP)
- Centre for Freshwater Ecosystems
- Research Centre for Applied Alpine Ecology

Many of our staff are members of one of the University's flagship Institutes:

- La Trobe Institute of Sustainable Agriculture and Food (LISAF)
- La Trobe Institute for Molecular Science (LIMS)

Or research centres:

- ARC Centre of Excellence in Plants for Space
- ARC Industrial Transformation Research Hub for Protected Cropping
- Industrial Transformation Research Hub for Molecular Biosensors at Point of Use (MOBIUS).
- Mallee Regional Innovation Centre (MRIC)(a joint venture with The University of Melbourne)

Professor Robyn Murphy
Dean, School of Agriculture, Biomedicine and Environment

Baker Department of Cardiovascular Research, Translation & Implementation

The partnership between the Baker Institute, an independent, internationally renowned medical research facility more than 95 years old, and La Trobe University has led to the establishment of the Baker Department of Cardiovascular Research, Translation and Implementation led by Professor Peter Meikle. Together, we are growing the scope, volume and quality of cardiovascular and diabetes research and are enhancing access to health service and research networks in academia, industry and government, including local and rural collaborations. Our research extends from the laboratory to wide-scale community studies. We focus on diagnosis, prevention and treatment of diabetes, cardiovascular disease and associated metabolic diseases. We offer postgraduate opportunities via our Honours, Masters and PhD programs, in fundamental science using preclinical models, clinical studies and epidemiological and public health studies. Our research aligns with La Trobe's research themes: Understanding and preventing disease and Healthy people, families and communities. Our researchers are experts in cardiovascular disease, diabetes and public health. Together, we are translating our discoveries into practice, policy and education. Our research is grouped into three key areas:

Clinical Research

We are identifying new and improved ways of preventing, diagnosing and treating heart disease and diabetes, and their complications. The goal is to enhance health, reduce disability, improve quality of life and address health disparities. Our work spans human and clinical research. Our scientists use imaging and other diagnostic tools to better inform our understanding of disease development and treatment. They also conduct clinical trials to evaluate new treatments and undertake health services research to inform how health care can be best delivered. Many of our researchers are also clinicians who work in a clinic or hospital setting. They are predominantly heart and diabetes specialists whose research is informed by the needs of their patients.

Discovery and Preclinical research

We are designing new diagnostic, preventative and therapeutic strategies to tackle cardiovascular disease, diabetes and its complications. We are working to understand the cellular mechanisms of disease, biomarkers in the progression of disease and the pathways of gene expression. Our work spans the Institute's laboratory-based cellular and molecular biology and preclinical research, with a focus on translating exciting discoveries in the laboratory to clinical care.

Population Health

We are examining trends in diabetes and obesity prevalence and incidence, risk factors at a population level, and new therapeutic approaches to prevent and treat diabetes, heart disease and obesity. Our research encompasses the Institute's epidemiological and public health groups, spanning clinical diabetes and obesity, physical activity, population health and behavioural epidemiology. Our work is helping to inform policy guidelines, influence chronic disease management, offer new evidence-based therapies for health professionals, and inform government and health authorities about the scale of these health problems. Our graduate researchers learn from world class experts in world class facilities.

Graduate research

Our Honours, Masters and PhD students work on projects alongside researchers, in scientific laboratories or research units that are closely connected with clinical facilities and focus on the translation of findings into improved health outcomes. They are well supported and recognised by dedicated awards and funding opportunities overseen by the Research Training and Education Committee, all designed to support and enhance the learning experience.

Partnerships

Together, we are growing the scope, volume, and quality of cardiovascular and diabetes research. We are enhancing access to health service and research networks in academia, government, and industry, including local and rural collaborations already developed by each organization.

Australian Partnerships:

We have a physical presence at several health care settings – ensuring our education and research programs are contemporary and meet the needs of our communities. This presence also allows us to collaborate with health professionals on innovative teaching and translational research.

International Partnerships:

We are globally connected through a range of formal partnerships and informal collaborations arrangements that strengthen our research capacity and outcomes. The Baker Heart and Diabetes Institute, for example, has partnered with University of Cambridge to establish the Cambridge Baker Systems Genomics Initiative. This transnational research partnership brings computational biologists together to drive the development of next-generation analytics, game-changing biology, and clinical utility from multi-omic datasets.

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 comprises a class of 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 observed 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.

Our research spans the spectrum of cardiovascular biology and diseases, encapsulating basic mechanistic research, clinical and allied health research, and epidemiological studies.

Work in our laboratories involves all major technologies of modern biomedical sciences with unique strengths in experimental animal models, mouse genetics, immunology, genomics and drug discovery, enabling translation of our findings into new diagnostics, preventions and treatments for cardiovascular disease. More specifically, the scope of our cross-disciplinary research includes:

- Unravelling the role of inflammation and activation of the immune system in the pathogenesis of hypertension and chronic kidney disease.
- Studying the inflammatory mechanisms occurring in the brain after a stroke or as a result of reduced blood supply due to stenosis of the carotid arteries.

- Examining changes in contractile properties of the heart during disease and how this is affected by sex hormones.
- Characterising the changes in the gut microbiome during hypertension, diabetes and stroke and determining how these changes influence disease progression.
- Investigating the role of foetal programming in the development of cardiovascular disease.
- Determining the functional components of diet that may protect against or increase the risk of developing cardiovascular disease.
- Utilising 'big data' statistical approaches to reveal associations and relationships between experimental variables and disease parameters, as well as risk factors for cardiovascular events from de-identified hospital and clinical data.

We strive for:

- Research Excellence; by integrating a range of disciplines, using cutting-edge multi-disciplinary technologies, and employing best practice in experimental design, to define the causes of cardiovascular disease and stroke.
- Collaboration; with world-leading researchers working in universities, hospitals and medical research institutes around Australia and across the globe.
- Being future-focused; we want to recruit, support and train the next generation of scientists committed to solving the most pressing global health problems.
- Impact; by partnering with government, the pharmaceutical industry and biotech, NGOs, philanthropic organisations, and communities, especially those in the north of Melbourne and regional Victoria, to share new knowledge and ensure it is translated into guidelines, diagnostics and therapies that reduce the socioeconomic burden of cardiovascular disease.

Co-Directors:
Prof Chris Sobey (c.sobey@latrobe.edu.au) and Prof Grant Drummond (g.drummond@latrobe.edu.au).
Group Leaders:
Prof Garrie Arumugam (Vascular Dementia); Dr Alex Pinto (Cardiac Cellular Systems); Dr Antony Vinh (Immunity and Hypertension); Dr Helena Kim (Stroke and Brain Inflammation); Dr Maria Jelinic (Obesity and Diabetes); Dr Michael De Silva (Cerebrovascular Disease).
Strategic Partners:
Australian Cardiovascular Alliance
Baker Heart and Diabetes Institute
Beluga Foundation.

Research Groups

Atherothrombosis and Vascular Biology Lab

The Atherothrombosis and Vascular Biology laboratory pursues a broad range of projects that have the common focus on improving diagnosis and therapy of thrombotic and inflammatory diseases such as myocardial infarction and atherosclerosis. A range of biotechnological methods are used, including recombinant protein design/production, generation of functionalised nano-particles/lipsomes/ microbubbles, cell culture, flow cytometry, flow chamber, microfluidics, intravital microscopy, ultrasound, MRI, PET various fluorescence imaging systems and various animal models of thrombosis, atherosclerosis and inflammation.

We have extended our research beyond cardiovascular applications, based on the successful application of our biotechnological tools for the targeting of activated platelets towards diagnosis and therapy of autoimmune diseases, such as multiple sclerosis, and cancer.

Most recently we are using our bio¬techno-logical expertise to develop mRNA therapies.

All of these projects have a strong translational orientation, which is facilitated by several laboratory members (physicians/ cardiologists/haematologists) treating patients with cardiovascular and haematological diseases as well as cancer. Several of the research projects resulted in patents that are currently being further translated to ultimately improve the health of patients.

Work in the laboratory is particularly attractive for students and postdoctoral researchers who are interested in the development of advanced biotechnological tools for molecular imaging and novel therapeutics (e.g., nanoparticles and anti-inflammatory drugs for plaque stabilisation). The translational direction of the laboratory and the inclusion of patients in studies is highly attractive for physician scientists.

Research focus

- Molecular imaging of thrombosis and inflammation using MRI, PET, ultrasound, FLECT, IVIS.
- Novel recombinant therapeutics for thrombotic and inflammatory diseases.
- Microfluidic flow chambers.
- Intravital microscopy.
- Flow cytometry.
- Animal models of thrombosis and inflammation.
- Production of recombinant proteins for diagnosis and therapy.
- Diagnosis and treatment of patients with coronary artery disease and myocardial infarction.
- Development of mRNA therapeutics

Lab Head: Professor Karlheinz Peter (k.peter@latrobe.edu.au)

Lab members:
Dr Sara Baratchi, Ms Viktoria Rose Bongcaron, Dr Yung-Chih (Ben) Chen, Dr Lisa M Domke, Ms Angela Huang, Dr Smriti Krishna, A/Prof James McFadyen, Dr Mitchell Moon, Dr Jonathan Noonan, Ms Prerna Sharma, Dr Anna Watson, Dr Johannes Zeller, Ms Julia Skoraczynski, Dr Nalin Dayawansa, Ms Shengyuan Liu, Ms Shania Anggita Prijaya, Dr Hanna Stevens, Dr Wen-Kai Wong, Mr Aidan Walsh, Ms Runali Patil, Ms Najma Fithri, Dr Abbey Willcox, Ms Samantha Loong, Ms Huiting Niu, Mr Thomas Montibeller, Ms Habiba Danish.

Fields of Study:
Cardiovascular Diseases, Atherothrombosis, cellular mechanisms of coronary artery disease and its consequences, myocardial infarction.

Capabilities and Techniques:
Ultrasound, MRI, PET, MicroCT, fluorescence and photoacoustic imaging; Generation of antibody-drug fusion constructs; mRNA; Cardiovascular murine models.

Translational Opportunities:
Early detection and prevention of CVDs; Targeted drug delivery; Gene therapy. We work closely with biotech companies to translate our research into clinical settings.

Cardiac Cellular Systems Lab

Heart failure is a leading cause of mortality worldwide.

Resulting from a wide range of aetiologies, heart failure is characterised by deleterious cardiac remodelling and decline in heart function, ultimately leading to organ failure and death.

Currently there are no effective treatments for heart failure, and fundamental questions remain unanswered regarding the ways in which cardiac remodelling occurs and how it may be reversed.

Until recently the cellular composition of the heart was poorly defined.

Using advanced genetic, flow cytometric and single cell transcriptomic approaches, our lab has shed new light on the cellular constituents of the heart by demonstrating that the heart is comprised of a complex and diverse ecosystem of non-myocytes.

Based on these discoveries, new avenues of cardiovascular research involving the targeting and manipulation of specific cell types and networks are now possible.

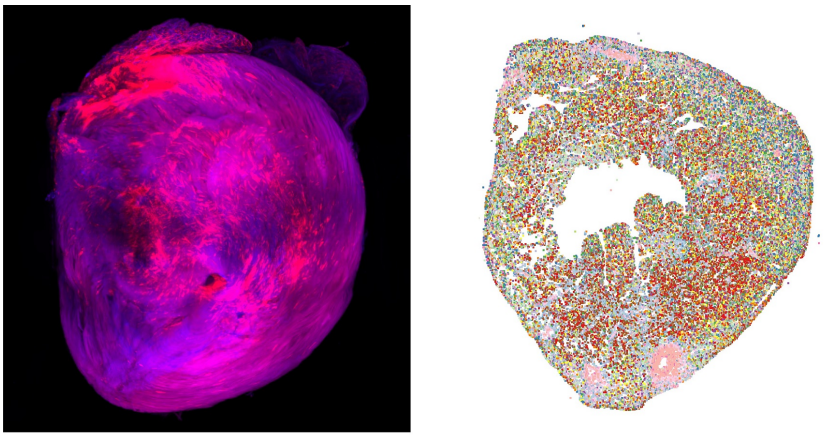
Today, very little is known about how the ecosystem of non-myocytes in the heart operate as a cell network.

Combining advanced single-cell omics, imaging and mouse genetics, our lab aims to study the complex ecosystem of cells that form the heart, to identify novel drivers of cardiac ageing and disease.

Overarching goals

1. Use single-cell genomics, high-resolution imaging and mouse genetics to map drivers of cardiac pathology.

2. Develop new drugs—nanoparticles and small molecules—to treat cardiac pathology and/or regenerate the heart.



(Left) 3D light-sheet microscopy image of the mouse heart after a heart attack. Red colour indicates nanoparticle-targetted cells. (Right) spatial transcriptomic image of the heart, profiling transcripts corresponding to ~30,000 genes.

Key areas of ongoing research

1. Determine how cardiovascular stressors such as obesity, hypertension and myocardial infarction impact cardiac cell networks

2. Determine how novel environmental hazards—such as micro- and nano-plastics—impact cardiac cell networks and broader cardiovascular physiology.

3. Development of new drugs to prevent development of cardiac fibrosis.

4. Development of new nanoparticles to target cardiac cells.

5. Development of new drugs and methods to regenerate the heart after myocardial infarction.

6. Determine sex-differences in cardiac development, homeostasis and disease.

7. Development of unique genetic, computational biology, and imaging approaches to precisely study diverse cell populations in of the heart.

Lab Head:
Associate Professor Alex Pinto
(a.pinto@latrobe.edu.au)
(alex.pinto@baker.edu.au)

Lab members:
Dr Patrick Lelliott, Dr Rebecca Harper, Dr Malathi Dona, Ms Gabriella Farrugia, Mr Crisdion Krstevski, Mr Thomas Harrison, Mr Ian Hsu.

Fields of Study:
Cardiac Cell networks; cardiology; heart disease; computational biology; nanochemistry.

Capabilities and Techniques:
1. Single cell biology — including single-cell RNA sequencing, high-dimensional flow cytometry and image cytometry.
2. Multidimensional imaging — including 3D imaging and spatial mapping of cellular interactions.
3. Mouse genetics — including development of novel cell- and organ-specific genetic tools.
4. Nanochemistry and cellular targeting.

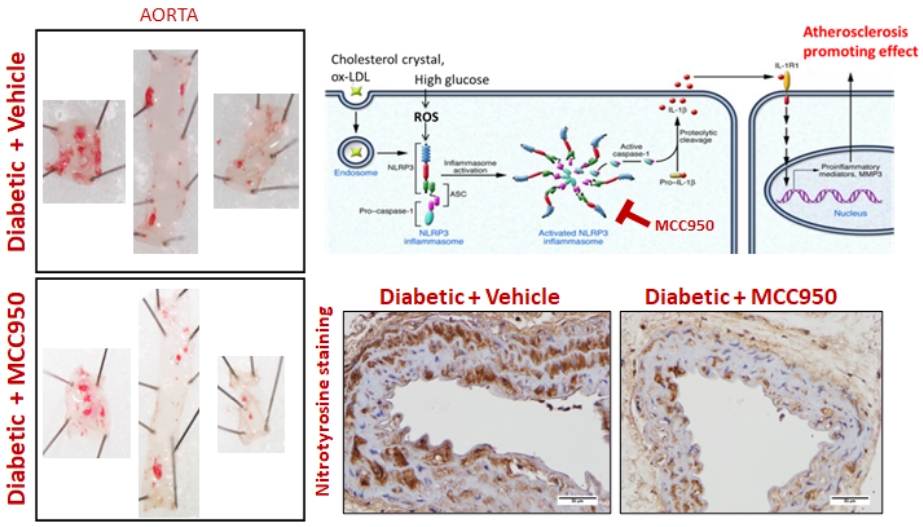
Translational Opportunities:
Development of new approaches to target molecular and cellular drivers of cardiac pathology. These include pharmacological, gene therapy and cellular approaches to address cardiac fibrosis, vascular dysfunction and inflammation.

Cardiovascular Inflammation and Redox Biology Lab

Our Laboratory investigates the pathways that drive cardiovascular complications of diabetes. Patients with diabetes are 2-4 times more likely than non-diabetics to experience a heart attack or a stroke, have high blood pressure, and present with vascular disease such as atherosclerosis. Patients with diabetes are also more likely to require balloon-angioplasty and stenting (BAS) to open blocked arteries (restenosis). Diabetes, via disruptions of major metabolic and immunological pathways, results in robust oxidative and inflammatory responses. Despite positive outcomes in preclinical settings, vitamins have not been efficacious in the clinic. Our novel approaches bolster the body's natural antioxidant defenses via compounds that regulate a transcription factor Nrf2, the master regulator of antioxidant and anti-inflammatory responses. We also target the NLRP3-inflammasome, a key cytokine-producing platform as well as downstream of the infammasome at the level of the GasderminD pore. Results from our preclinical mouse models are yielding promising reductions in micro- and macrovascular complications.

Nrf2 activators

Our Lab has a strong track record of studying the activators of Nrf2 as a therapeutic strategy to lessen not only oxidative stress, but to additionally dampen diabetes-driven inflammation. Together with our industry partner Reata Pharmaceuticals, and using their tool compound dh404, we have shown significant reductions in diabetes-associated atherosclerosis. This is via reductions in oxidative stress and a direct effect on the NLRP3 inflammasome. Further mechanistic understanding is required to fully validate this new approach to control diabetes-mediated atherosclerosis. Further, how these drugs control restenosis is an ongoing investigation in our laboratory.



Sharma A...de Haan J.B. Specific NLRP3 inhibition protects against diabetes-associated atherosclerosis. ***Diabetes,*** 70:772-787, 2021.

NLRP3 inhibitors

We have investigated a small molecule inhibitor of the NLRP3-inflammasome (MCC950) and its ability to improve diabetic macrovascular complications such as diabetes-associated atherosclerosis. Our extensive programs now allow us to investigate its use in improving other diabetic complications including endothelial dysfunction, restenosis, and post myocardial infarction.

GasderminD pore

Targeting the key cellular regulator of pyroptosis is a novel approach to limiting the damage that results in diabetic micro- and macrovascular complications. Our results with a known GasderminD inhibitor are showing promising results in bone marrow derived macrophages. We now have a range of untested and prioritized potential inhibitors ready for further testing, designed using the Baker Institute Computational Biology platform. This project will generate new drugs for the treatment of diabetic cardiovascular diseases.

Lab Head: Professor Judy de Haan (j.dehaan@latrobe.edu.au)

Lab members:
Dr Arpeeta Sharma;
Judy Choi (PhD student);
Nada Stefanovic (Senior Research assistant).

Fields of Study:
Diabetes; Atherosclerosis; Stent Biology; Oxidative Stress; Inflammation.

Capabilities and Techniques:
Cell culture of mouse and human endothelial, smooth muscle and bone-marrow derived macrophages; Robust animal models of diabetes and atherosclerosis; qRT-PCR; Western blotting; ELISA; histology; immunohistochemistry; immunofluorescence; stent surgeries

Translational Opportunities:
New drug discovery based on in-depth understanding of the oxidative and inflammatory mechanisms under-pinning diabetic complications.

Clinical Diabetes and Epidemiology Lab

The Clinical Diabetes and Epidemiology group has two main focuses. The first is the epidemiology of type 2 diabetes, examining trends in prevalence and incidence of diabetes (predominantly type 2) in Australia and the rest of the world. The work in this area, pioneered by Prof Paul Zimmet, has been instrumental in demonstrating the rapid growth of the emerging global diabetes epidemic. The surveys undertaken for this work also provide rich data for interrogating a range of putative and novel risk factors for diabetes and its complications, of which lifestyle factors have been studied extensively and remain an important target. The second focus capitalises on the large patient population in our Diabetes Clinic. This facilitates examination of novel treatments, and of observational data on real world responses to therapies.

Diabetes complications cohort study

A cohort study, called PREDICT, focusing on the development of diabetes complications is currently recruiting participants. It will recruit 2000–3000 people with type 2 diabetes, and aims to better understand the causes of the complications of diabetes. This study will examine not only the classic complications of eye, kidney, nerve and cardiovascular disease, but will also examine emerging complications, such as cognitive decline and frailty. Central to the study is the establishment of a biobank of samples that can be interrogated for a variety of novel candidate causes of the complications of diabetes. A sister study, PREDICTION, is currently being initiated. This will focus on the rapidly-developing epidemic of type 2 diabetes in younger adults. Younger-onset type 2 diabetes has been associated with poorer outcomes than diabetes with the more usual onset in middle-age. Like PREDICT, it will be a population-based cohort, and will examine the complications of diabetes. It will also include a cohort of people with adult-onset type 1 diabetes, which is another sub-group in diabetes about which knowledge is very limited.

Data linkage studies

For the last ten years, we have undertaken large data linkage projects. The NDSS is a register of approximately 80-90% of all people with diabetes in Australia. Although limited data are held in the NDSS, linking it to Medicare prescription databases, the National Death Index, the dialysis and kidney transplant registry and to hospital admission datasets provides a powerful tool for examining the population-level impact of diabetes and its complications. We examine the burden of diabetes complications, trends in diabetes and its complications, disease costs, and the impact of socio-economic status on diabetes and its complications.

Global diabetes registry analyses

We established and lead the GLOBODIAB collaboration, which brings together national and sub-national diabetes registries from over 20 countries around the world. This powerful set of data, with information on tens of millions of people with diabetes allows comparisons between countries for important aspects of diabetes epidemiology, such as the trends in in the incidence of and mortality in diabetes, the distribution of causes of death, and the risks of developing important complications.

Australian Diabetes Obesity and Lifestyle Study (AusDiab)

The Australian Diabetes, Obesity and Lifestyle Study (AusDiab) is the largest Australian longitudinal population-based study examining the natural history of diabetes, pre-diabetes (in which glucose metabolism is impaired but not to the level to cause diabetes), heart disease and kidney disease. The 1999/2000 AusDiab study was the first national diabetes prevalence study to be conducted in Australia, and included 11,247 adults from 42 different locations across Australia. The participants were followed up in 2004/2005 and again in 2011/12 to provide the first ever information about the incidence (or development) of diabetes and other non-communicable diseases in Australia over time.

Lab Head: Professor Jonathan Shaw, (j.shaw2@latrobe.edu.au), Professor Dianna Magliano (d.magliano@latrobe.edu.au).

Lab members: Dr Julian Sacre, Dr Lei Chen, Dr Elizabeth Barr, Dr Anne Reutens; Ms Maria Lawton; Ms Robyn Veljanovski; Mrs Elena Vulikh; Ms Alexandra Eckert; Mr Nicholas Johnson.

Fields of Study:
Trends in diabetes prevalence and incidence; type 2 diabetes and its complications at a population level; risk factors for diabetes complications.

Capabilities and Techniques: Establishment of population-based cohort studies; data linkage; advanced epidemiological analyses; access to large whole-of-population datasets.

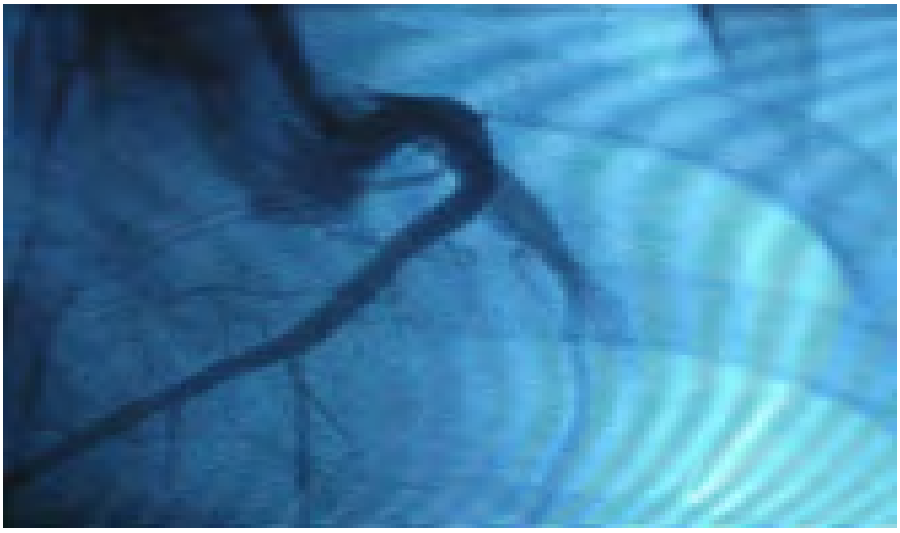
Translational Opportunities:
Data from our studies are translated into healthcare planning by providing robust estimates of disease burden.

Haematopoiesis and Leukocyte Biology Lab

The Haematopoiesis and Leukocyte Biology laboratory focuses on understanding the pathways contributing to enhanced leukocyte production and altered function in the context of (but not limited to) cardiovascular and metabolic diseases. Diets high in calories, saturated fat, and cholesterol combined with a sedentary lifestyle lead to a high prevalence of atherosclerotic cardiovascular disease (CVD). High-circulating blood lipids, including elevated low-density lipoproteins (LDL) and triglyceride-rich lipoproteins, result in increased entry and retention of these particles in the arterial wall, leading to a macrophage-dominated chronic inflammatory process and eventuating in atherosclerotic plaque rupture or erosion, myocardial infarction, or thrombotic stroke. While elevated plasma cholesterol levels have an essential role in atherogenesis, comorbidities such as smoking, hypertension, and diabetes accelerate atherosclerotic CVD.

In addition, chronic kidney disease, recurrent infections, myeloproliferative neoplasms, and autoimmune disease such as rheumatoid arthritis and systemic lupus erythematous also greatly increase the risk of athero- thrombosis. A common theme linking these diseases to athero- thrombosis is an overactive immune system, mediated in part by increased production and activation of innate immune cells. We seek to understand these changes in the immune system from the level of the long-lived haematopoietic stem cells through to the mature effector cells such as monocytes and macrophages.

We study fundamental biological process contributing to the retention and liberation of haematopoietic stem cells (HSCs) within specific bone marrow (BM) niches and how these HSCs and the BM niche become altered in disease. We are interested in how these HSCs traffic to the spleen and initiate extramedullary haematopoiesis. We focus on how inflammatory diseases associated with increased cardiovascular risk influence these pathways, including diabetes, obesity and autoimmune diseases such as rheumatoid arthritis. We explore how these diseases influence the function of circulating cells, (monocytes, neutrophils and platelets). We study the role of plaque macrophages and pathways contributing to foam cell formation. We are also exploring two main outcomes of vascular disease, myocardial infarction and stroke and how these diseases influence the haematopoietic system to promote enhanced myelopoiesis, which is associated with a worse outcome. We focus on exploring the utility or current treatments and developing novel therapies to target the pathways we have identified in our preclinical models that are also detect in patients with these diseases.



Using contrast dye to evaluate coronary blood flow (Photo credit: Colleen Thomas)

Research focus
Fundamental process regulating haematopoiesis.
Exploring how the lipidomes of immune cells regulates their function.
Understand multi-organ communication to stimulate haematopoiesis.
Determining how the body responds to hyperglycaemic spikes.
Exploring if and how inflammatory diseases associated with increased cardiovascular risk impair the regression of atherosclerotic lesions.
Understanding how enhanced reticulated platelets influence accelerated atherosclerosis in diabetes.
Exploring the role of human monocyte subsets in cardiovascular disease.
Investigating pathways contributing to foam cell formation in the atherosclerotic lesion.

Lab Head: Professor Andrew Murphy (a.murphy2@latrobe.edu.au).

Lab members:
Dr Dragana Dragoljievic;
Dr Andrew Fleetwood;
Dr Graeme Lancaster;
Dr Sam Lee;
Dr Pooranee Morgan;
Ms Camilla Bertuzzo Veiga;
Mr Patrick Bell;
Mr Tom Collins;
Mr Simon (Yangsong) Xu;
Ms Zoe (Yiyu) Zhang.

Fields of Study:
Cardiovascular Diseases; Inflammatory chronic metabolic disease; Haematology; diet/dietary lipids; immunometabolism.

Capabilities and Techniques:
Cell Culture; Molecular Biology; Animal Models; Biotechnology; Stem cell and mature effector cell research techniques.

Translational Opportunities:
Inflammatory disease therapies; Atherosclerotic lesion therapies for diabetes and other diseases.

Inflammation and Cardiovascular Disease Lab

The Inflammation and Cardiovascular Diseases laboratory uses a multi-disciplinary approach to understand how the immune system and inflammation modulate the pathogenesis of cardiovascular diseases.

Inflammation is a protective response triggered by damage to living cells.

This response localises and eliminates the injurious agents, while also removing damaged tissue components so that the body can heal and maintain homeostasis. In cardiovascular diseases, the injury may be caused by internal factors (e.g. myocardial infarction (MI) rather than external factors such as bacteria or viruses).

The immune system is largely responsible for initiating inflammation and untreated acute (subclinical) inflammation leads to chronic inflammation that eventually causes cell damage (e.g arteries).

Our areas of focus are vascular inflammation (atherosclerosis) and cardiac inflammation (cardiomyopathy).

We will decipher how both adaptive and innate systems contribute to inflammation in cardiovascular diseases in animal models.

We aim to translate these findings into practice in both diagnostics for early detection and therapeutics for effective intervention to prevent premature plaque ruptures.

Associate Professor Tin Kyaw

Current research projects:
Better understanding and preventing recurrent myocardial infarctions.

CD4+ regulatory T cells and preventing/ reversing the development of vulnerable atherosclerotic plaques associated with unstable angina and MI/stroke.

Understanding how gamma-delta T cells contribute to vulnerable plaque development.

Myocardial inflammation associated with myocardial infarction.

Diffuse interstitial cardiac fibrosis.

Lab Head: Associate Professor Tin Kyaw (t.kyaw@latrobe.edu.au)

Lab members:
Dr Kurt Brassington;
Mr Peter Kanellakis;
Ms Yi Ee Lye.

Fields of Study:
Immune system, inflammatory disease, cardiovascular diseases, stroke.

Capabilities and Techniques:
Cell Culture; Molecular Biology; Animal Models; Biotechnology; cell research techniques.

Translational Opportunities:
Diagnostics for early detection and therapeutics for effective intervention to prevent premature cardiovascular plaque ruptures.

Imaging Research Lab

The Imaging Lab is led by Professor Tom Marwick, who is involved in clinical research and research training. As a cardiologist, he has a focus on health outcomes and holds particular expertise in cardiac imaging in heart failure and coronary disease, and the detection of early stages of cardiac dysfunction.

He was one of the initiators of stress echocardiography, and has made contributions to the prognostic evidence underlying cardiovascular imaging. His research interests relate to the detection of early cardiovascular disease and cost-effective application of cardiac imaging techniques for treatment selection and monitoring.

The Imaging Research laboratory is dedicated to developing pathways for better integration of imaging with clinical management — including quality and appropriate use and cost-effectiveness of imaging, risk evaluation and intervention based on detection of early stage cardiovascular disease, heart failure with preserved ejection fraction, and new cardiovascular imaging modalities.

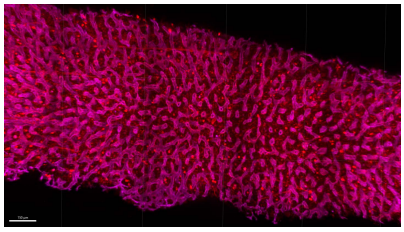
The research focus of the Imaging Lab is

- Risk evaluation and intervention based on detection of early stage cardiovascular disease.
- Heart failure with preserved ejection infarction.
- Quality, appropriate use and cost-effectiveness of imaging.
- New cardiovascular imaging modalities.

In conjunction with research work the lab is heavily focused on these clinical research studies:

CAUGHT-CAD
A multi-centre Australian randomised trial of coronary calcium for risk evaluation and prevention in patients with a family history of coronary artery disease.

Heart failure readmission
This study is based on the ability of echocardiography to assess haemodynamics and myocardial function, we aim to reduce heart failure admissions and costs



SUCCOUR
We aim to show that cardiac imaging surveillance leads to the use of adjunctive cardioprotective therapy that will limit development of reduced ejection fraction at one-year post chemotherapy (primary outcome), and interruptions to planned chemotherapy and the development of heart failure in follow-up (secondary outcomes).

TAS-ELF and VIC-ELF
This study is on Early LV Dysfunction and atrial fibrillation in Tasmania and Victoria. These are an observational dataset (TasELF) and an RCT (VicELF) that seek to provide early diagnosis and treatment to prevent the progression of asymptomatic to symptomatic heart failure.

AGILE
This study is on the use of Artificial Intelligence-Guided Echocardiography to Guide Cardiovascular Management in Rural and Remote Australia.

ARISE-HF study
This study looks at the complications diabetes can cause, including heart damage. It is a multi-centre, randomised placebo-controlled study to evaluate the safety and efficacy of an investigational drug in patients with diabetic cardiomyopathy/Stage B heart failure.

AMEND-CRT trial
This trial aims to improve selection of heart failure patients for this expensive and potentially harmful intervention of Cardiac Resynchronization Therapy (CRT), which is used as a treatment option in addition to standard medical therapy for patients with reduced left ventricular function and a clear conduction delay.

ED-CAD
This study is on the Early detection of coronary artery disease by polygenic and metabolic risk scoring (EDCAD-PMS) aims to identify whether a polygeneic risk score (PRS) can predict the presence of coronary calcium in the arteries, which occurs when plaque is present. We also want to find out whether knowing your PRS or knowing the results of your CT angiogram (a scan of your coronary arteries) is more effective at reducing cardiovascular risk/

PERCEIVE
This study aims to understand whether COVID-19 causes damage to the heart and impacts functional capacity. We also want to know if best practice management (e.g. heart medication or exercise training) can restore function/

RISK-HELP
Risk-guided strategy for reducing readmission for Acute Decompensated Heart Failure (Risk-HELP). We aim to identify whether a targeted management plan focusing on control of the body's fluid volume, phone and personal follow-up, home surveillance through a Heart Failure app on your smart phone and home treatment can reduce repeat hospital admission in heart failure patients.

Lab Head
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Lab members:
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Fields of Study:
Cardiovascular Disease

Capabilities and Techniques:
Cardiac Imaging

Translational Opportunities:
Detection of early cardiovascular disease and cost-effective application of cardiac imaging techniques for treatment selection and monitoring.

Metabolomics Lab

Our laboratory applies state of the art lipidomic capabilities to characterise the relationship between lipid metabolism and cardiometabolic disease. Clinical translation of our research will deliver new diagnostic/ risk assessment/monitoring tests and therapeutic interventions for chronic disease. Dysregulation of lipid metabolism underpins multiple diseases including obesity, type 2 diabetes, cardiovascular disease and age-related dementia. We have utilised tandem mass spectrometry to develop the only high throughput lipidomic platform in Australia and have performed some of the largest clinical and population lipidomic studies yet reported.

These have enabled the characterisation of metabolic pathways and identified lipidomic biomarker profiles that are able to better predict disease risk and therapeutic efficacy. Modulation of the same pathways now holds potential as an interventional strategy to prevent, attenuate or treat the major chronic diseases. Our areas of focus are:

- Population metabolism and biomarker discovery
- Lipidomic/Genomic integration to identify causal pathways to metabolic disease
- Preclinical/mechanistic studies in metabolic therapy
- Translational metabolomics — new therapies for metabolic disease
- Development of lipidomic and metabolomic capabilities in Australia

Our research program aims to characterise the environmental and genetic influences on metabolism and provide the fundamental understanding to select the optimal biomarkers for risk assessment and monitoring of therapy and to assist in the development of policy in order to maintain metabolic health in an aging population. Our developing translational pipeline through academic and commercial partners will enable us to realise the clinical translation of these new biomarkers.

Genetic determinants of lipidomic variation and their role in CVD risk

There is emerging evidence that rare genetic variation is a likely contributor to heritable risk of cardiovascular disease (CVD,) which is the leading cause of death in the world. We utilise large empirically defined Busselton Health Study family lineages to identify rare causal variants for CVD. We hypothesise that genetic analysis of the plasma lipidome in large families enriched for CVD events, with a focus on identifying rare mutations, will identify novel CVD risk factors of large effect. These risk factors will have clinical utility in the diagnosis and prediction of CVD.

Identifying lipid and genetic signatures of metabolic disease in early childhood

The antenatal period and early childhood offer a critical window of high plasticity and potential for early intervention to prevent the onset of adverse health trajectories. We hypothesise that plasma lipidomic profiles, combined with genomic profiles, will facilitate the identification of those individuals on adverse health trajectories and provide mechanistic insight to guide preventative interventions. Utilising two unique birth cohorts from Singapore and Australia, we aim to identify early childhood markers of metabolic disease which may herald future risk for development of type 2 diabetes and cardiovascular disease. We also aim to elucidate novel molecular mechanisms with the potential to underpin new therapeutic approaches for the prevention and management of metabolic diseases.

Lipidomic analysis of Alzheimer's disease; biology, risk assessment & early diagnosis

There is currently no cure for Alzheimer's Disease (AD) and treatment options are limited. A key factor in the development and implementation of AD therapies will be the early identification of those affected or of likely to become affected by AD. Studies have identified lipids as putative biomarkers of AD risk. Our research aims to understand the complex relationships between lipid metabolism and dementia to provide new therapeutic targets for early intervention to halt the onset and progression of AD.

Lab Head: Professor Peter Meikle (p.meikle@latrobe.edu.au)

Lab members: Dr Anjali Bhagwat; Dr Habtamu B Beyene; Dr Satvika Burugupalli; Dr Aleksandar Dakic; Dr Alexandra George; Dr Corey Giles; Dr Kevin Huynh; Dr Thomas Meikle; Dr Sudip Paul; Dr Tingting Wang; Dr Jingqin Wu; Dr Joe Yi.

Fields of Study:
Metabolomics; Cardiometabolic disease; Lipid metabolism; Biomarkers.

Capabilities and Techniques:
Defining new lipidomic biomarker profiles for chronic disease; identifying genes controlling lipid homeostasis; mapping lipid metabolic pathways involved in chronic disease; identifying regulatory mechanisms (therapeutic targets) . Tandem Mass spectrometry; study design; Lipid extraction; Liquid chromatography mass spectrometry; Data extraction and analysis.

Translational Opportunities:
Clinical translation and commercialisation of lipidomic biomarkers as well as nutraceutical and therapeutic products.

Molecular Imaging and Theranostics Group

Our Group focus is on providing better diagnostic imaging, side-effect free targeted drug/mRNA delivery and theranostic (concurrent therapy and diagnostics) approaches for a range of cardiovascular diseases. The team's research involves:

1) Advanced functional and molecular imaging of cardiovascular diseases using ultrasound, MRI, PET, MicroCT, fluorescence and photoacoustic imaging.
2) Biotechnology for genetic design and engineering of recombinant proteins, as well as antibody-drug fusion therapeutics for cardiovascular diseases.
3) Biomaterials selection, design, functionalisation and generation of innovative nano-/micro-particles for drug/mRNA delivery.
4) Novel conjugations of antibody-particles using biological and/or chemical coupling.

Work in this laboratory is particularly suitable/would be ideal for students and postdoctoral researchers who are interested in the development of advanced biotechnological tools for molecular imaging and novel therapeutics (e.g. nanoparticles). The translational direction of the laboratory and the inclusion of patients in studies is highly attractive for physician-scientists.

Molecular Imaging

Clinical imaging technologies mainly provide an anatomical readout of the structural changes for diagnosis, usually after irreversible damage has occurred. Our research aims to advance a range of innovative preclinical imaging modalities for more sensitive functional readouts. The technologies employed include ultrasound, MRI, PET, MicroCT, fluorescence and photoacoustic imaging. Novel molecular imaging incorporates a range of techniques (biology, biotechnology, chemistry and physics) to achieve a more comprehensive diagnosis and enable early detection of cardiovascular diseases.

Targeted drug/RNA delivery

Clot-busting drugs have frequently been associated with side effects of potentially life-threatening bleeding complications, thereby limiting their wider clinical use. Our research focuses on the development of recombinant antibody-drug fusion constructs for targeted drug delivery. This approach directs therapy to the desired site of action, allowing for lower concentrations of effective systemic drugs to be used, thus eliminating the risk of side effects. Therefore, our targeted drug delivery approach has the potential to create a paradigm shift for side-effect free prophylactic and therapeutic use across a variety of CVDs. We also use mRNA therapeutics to stop the progression of chronic inflammation to prevent devastating CVD events from occurring.

Theranostics

Innovative theranostic strategy involves concurrent diagnosis and therapy. The use of targeted nano-/micro-particles gives us the flexibility to increase the therapeutic payload of drugs, including gene therapy. In our research projects, we design and develop biocompatible particles with improved contrast properties and enhanced loading of therapeutic agents.

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Lab members:
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Fields of Study:
Cardiovascular Diseases, Imaging, Targeted Drug/mRNA, Nanobiotechnology.

Capabilities and Techniques:
Ultrasound, MRI, PET, MicroCT, fluorescence and photoacoustic imaging; Generation of antibody-drug fusion constructs; Design and create nanoparticles and mRNA; Cardiovascular murine models.

Translational Opportunities:
Early detection and prevention of CVDs; Targeted drug delivery; Gene/mRNA therapy; Theranostics. We work closely with biotech companies to translate our research into clinical settings.

Molecular Proteomics Group

Our laboratory studies the molecular function of nano-sized biological extracellular vesicles (EVs) to deliver, reprogram and engineer strategies for cell/ tissue repair and regeneration. Our advanced nano approaches have identified novel signaling regulators. We utilize advanced quantitative mass spectrometry to study proteome regulation to unravel mechanistic insights, including how EVs mediate their function. Our research has led to important developments in delivery-based therapeutic applications for fatty liver disease, cardiac protection/repair, adopted internationally for clinical trials, multiple international patents, and industry engagement (CSL, Tithon Biotech, VivaZome, Prescient Therapeutics). We also study EV composition and function, EV surface/targeting capacity, and EV utility to design new deliverable therapeutics and nanoparticles for cell-free therapies.

Mechanisms of cell reprogramming by EVs
EVs intercellular communication influences most cell physiology processes. EV intercellular signaling enables complex instructions (transmitted via bioactive cargo) to be sent to specific recipient cells. However, due to their intricate molecular complexity, quantitative knowledge on their signaling mechanisms is missing, this impedes their biological interpretation and therapeutic application. We focus on studying EV-mediated cell signaling (phosphorylation) mechanisms and how these impact cell reprogramming and function of specific cells and multi-cellular organoid models of cardiac disease.

Surfaceome and targeted delivery of EVs
The EV surface proteome (surfaceome) is a fundamental signaling gateway that links intra- and extracellular signaling networks and enables EVs to communicate and interact with their environment. We found EV-mediated reprogramming of target cells alter their cellular landscape and surfaceome (surface proteome). Functionalization of EV surface proteins is an effective means to design vehicles that could deliver therapeutic drugs and nanocarriers to target sites. We study EVs as systemic regulators and focus on how they target cells and organs. We use EV surface expression/modification as a new way to target and deliver to the heart.

Defining circulating EV heterogeneity
Molecular dissection of circulating EVs in human plasma is essential for understanding EV function and disease biomarker discovery. We developed a strategy to purify circulating EVs and comprehensive proteomic and lipidomic characterization from clinically relevant plasma volume important for biomarker discovery, dissecting function and standardization of their protein/lipid landscape. We study the heterogeneity of different circulating EV and non-EV subtypes. We aim to investigate circulating EVs in coronary artery disease and identify how circulating EVs and whole plasma profiling can differentiate development of coronary atherosclerosis.

Cell-derived nanovesicles delivery platform
Red blood cell (RBC) membranes generate EV mimetics (nanovesicles). Their membrane proteome expresses surface proteins (e.g. CD47) that improve biocompatibility and bioavailability. We have found that RBC-derived nanovesicles are important for paracrine signaling in cell-based therapies and can be used as a drug delivery platform. EVs and nanovesicles from stem/progenitor cell-based models are used as standalone therapies for cardiac repair. We use molecular, cell and protein biology methods, as well as models of cardiac disease/damage to find biological pathways for EVs to deliver cardiac protection and repair therapeutics.

Spatial proteomics and cardiac remodeling
Mass spectrometry-based spatial proteomics has been used in profiling protein spatial dynamics at an organelle level. Proteins subcellular location impacts their biological functions (i.e. growth and proliferation, structural preservation, signal transduction, and cell movement). Systemic analysis of organelle-specific proteome and phosphoproteome changes reveal key insights in organelle composition and disease progression. We use spatial proteomics to study subcellular proteome and phosphoproteome changes in cardiac cell and tissue remodeling. We develop therapeutic strategies, to understand changes in subcellular dynamics that could complement known mechanisms of actions and reveal organelle cross-talk.

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Fields of Study:
Proteomics; Cell signaling; Extracellular vesicles; Cardiovascular Disease; Cell Biology; Nanovesicles.

Capabilities and Techniques:
Mass spectrometry; quantitative proteomics; phosphoproteomics; functional assays; comprehensive plasma profiling (proteomic); informatics; density fractionation; EV characterization (biochemical and biophysical)

Translational Opportunities:
Native/biological EVs properties offer stability and aid crossing biological barriers to deliver molecular cargo to cells, acting as intercellular communication to regulate function and phenotype. We have defined the EV surface, signaling and cell reprogramming molecular mechanisms, and led discoveries on EV heterogeneity in blood. Our EV design advances and engineering methodologies facilitate development of therapeutics for cardiovascular diseases. We translate research discoveries in partnership with biotechnology and preclinical companies.

Non-Communicable Diseases and Implementation Science

Our laboratory aims to make a meaningful difference to the lives of people living with chronic conditions. We also aim to increase the research capacity and expertise in the prevention and management of non-communicable diseases (NCDs) at the national and international level in both high- and low/middle income countries where we work. Our work generates high quality evidence to inform policy and practice and we develop effective evidence-based solutions that improve health outcomes of people with non-communicable diseases. Our international team, leads and collaborates on a variety of multidisciplinary research, evaluation, quality improvement, and science implementation projects. Our community of professionals in NCD prevention and control consists of researchers, healthcare practitioners, policymakers, and members of the public. Our cutting-edge advantage is we work collaboratively across disciplines, countries, settings, seniority levels to implement interventions, programs and policy changes that improve health in Australia and beyond. We are passionate about effective, cost-effective, and equitable health improvement at the population level. We strive to implement evidence-based health solutions across contexts and settings.

Long-term effects of a structured lifestyle intervention on cardiometabolic risk
The Kerala Diabetes Prevention Program is a cluster-randomized controlled trial of 1007 individuals conducted Kerala state, India. We aim to examine the effects of a lifestyle intervention on blood pressure, blood glucose, obesity, and cholesterol levels using data on sociodemographic characteristics, behavioral/lifestyle factors, medical history, family history of disease, health service utilization, psychosocial variables, anthropometric and biomedical measures. Data were collected at baseline, 12 months (at completion of intervention), and 24 months. Data collection for the 8th year follow-up will be completed in 2022.

Scaling up structured lifestyle interventions to improve hypertension & diabetes control
In partnership with the governments of Kerala and Tamil Nadu and leveraging India's national NCD program, this

NHMRC-GACD funded project's implementation stage is being undertaken by the National Institute of Epidemiology (Tamil Nadu), Sree Chitra Tirunal Institute for Medical Sciences and Technology (Kerala), in collaboration with the Baker Heart and Diabetes Institute. This project aims to find evidence-based research on the scale up of lifestyle modification interventions to control Type 2 diabetes and hypertension.

Codesigning adaptations to digital healthcare delivery for people with acute coronary syndrome: Smart-CR
This proof-of-concept program involves a large interdisciplinary research team that disseminates findings through seminars and publications. The research program provides urgently needed cost-effective, convenient, accessible, sustainable, and scalable virtual delivery of healthcare service at home. Our unique technology-enabled healthcare delivery platform will provide a digital ecosystem of individually tailored support and healthcare services delivery to people with chronic and complex medical conditions and/or disabilities.

Implementation research capacity strengthening
Our NCD and Implementation Science laboratory conducts capacity-building programs to strengthen implementation research and includes technical assistance and consultancy. Our resources include:
Implementation research e-Hub
With GACD support, we developed an online implementation research science e-Hub focused on chronic and complex NCDs. This online learning space for gaining new knowledge and building on skill development has been instrumental in conducting implementation research training and development;
Implementation Science School
Our team co-leads the annual Implementation Science School with GACD. Up to fifty early- and mid-career researchers, practitioners and policy makers attend the school;
Implementation Research Workshops
We run workshops and short courses in collaboration with other leading academic and research institutions in low and middle-income countries, including the Institute for Health System Research (Malaysia) and the University of Philippines.

Connected Health NHMRC Centre of Research Excellence
Prof Oldenburg is the PI/Director of this CRE which aims to develop and implement technology to improve health care delivery and health outcomes for people with long term chronic conditions. Our team participates in this Centre's Career Development Program which involves research and health service collaborators worldwide.

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Fields of Study:
Non-communicable diseases; Chronic disease management: Digital Health; Health Behaviour.

Capabilities and Techniques:
Implementation science

Translational Opportunities:
Digital chronic disease management.

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