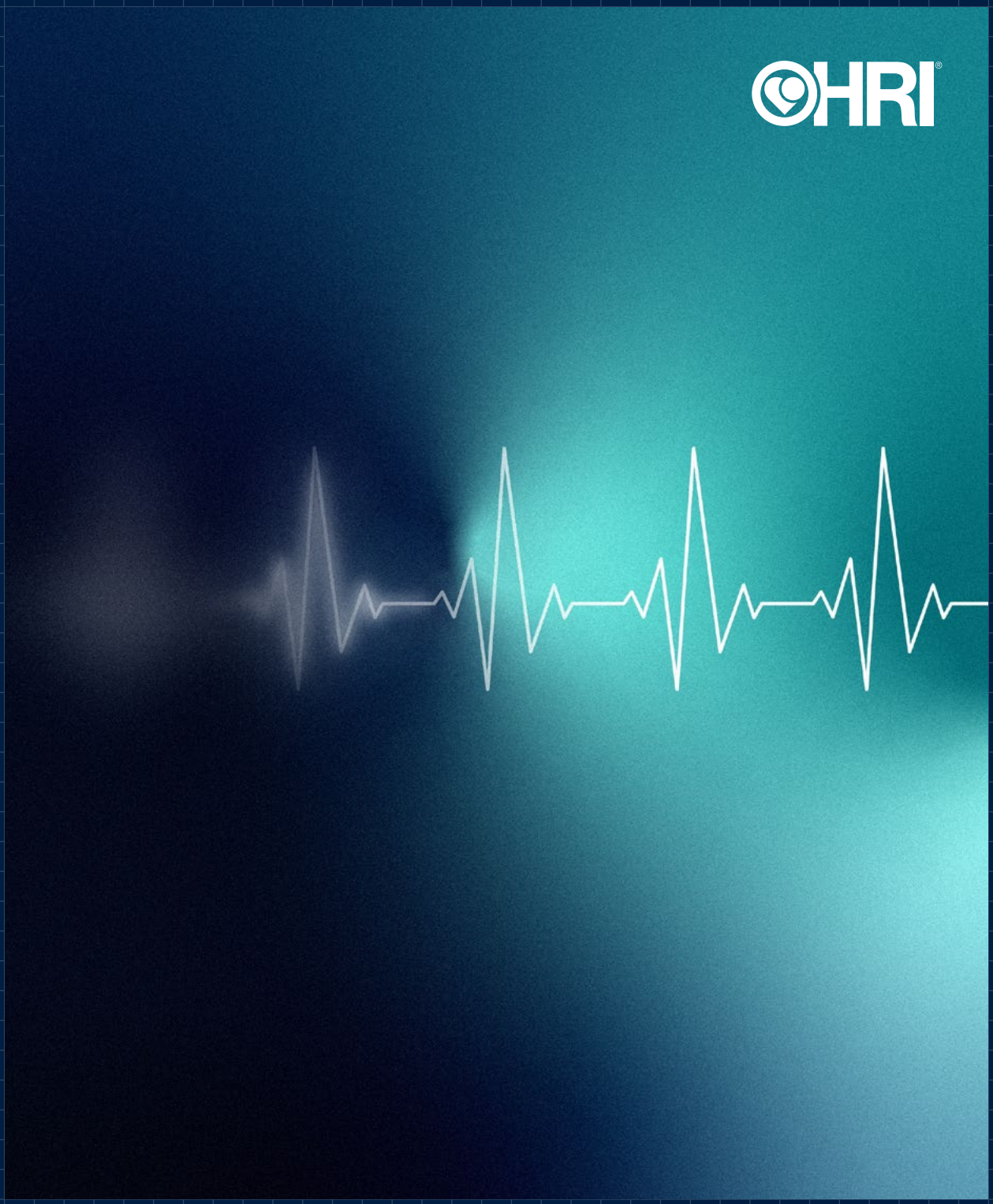
Heart Research Institute
2020 Annual Review



Navigating 2020

WITHOUT SKIPPING A BEAT

Despite the challenges of 2020, our generous supporters and dedicated researchers continued our crusade to beat cardiovascular disease.

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Dr Marc Ellis, Thrombosis Group

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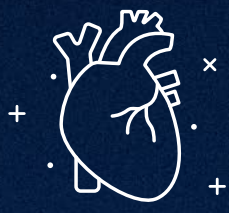
Our Mission

HRI's mission is to prevent death and suffering from cardiovascular diseases, a complex array of diseases affecting the heart and blood vessels. We will address areas of unmet need in cardiovascular diseases, including coronary artery disease, stroke, peripheral artery disease, hypertension, heart failure, preeclampsia, congenital heart disease and pulmonary vascular disease, as well as metabolic complications such as diabetes.

Specifically, our research programs will:



Provide greater understanding of the pathogenesis, development and early detection of cardiovascular diseases

Develop new drug therapies and devices to prevent and treat cardiovascular diseases and translate these through to clinical trials

Train the next generation of cardiovascular research leaders

Connect cardiovascular research communities to maximise collaboration and research translation

Imala Alwis, Thrombosis Group

LOCATIONS

7 Eliza Street, Newtown, Sydney

Charles Perkins Centre,
The University of Sydney,
Camperdown, Sydney

14 SCIENTIFIC GROUPS

Arterial Inflammation and Redox Biology
(joined November 2020)

Atherosclerosis and Vascular Remodelling

Cardiometabolic Disease

Cardiovascular Medical Devices

Cardiovascular Neuroscience

Cardiovascular-protective Signalling and Drug Discovery

Clinical Research

Coronary Diseases

Haematology Research

Heart Rhythm and Stroke Prevention

Microvascular Research
(joined November 2020)

Thrombosis

Vascular Complications

Vascular Immunology

Chair
Professor Len Kritharides

Director of Cardiovascular Research
Professor Shaun Jackson

Chief Executive Officer
Dr Stephen Hollings

Deputy Director Research Strategy
Professor Ben Freedman OAM

Scientific Director
Emeritus Professor Carolyn Geczy

Clinical Director
Professor David Celermajer AO

Associate Directors of Research Management and Education
Dr Mary Kavurma (Eliza St)
Associate Professor Simone Schoenwaelder
(Charles Perkins Centre)

OUR PARTNERSHIPS

Sydney Local Health District and Sydney Health Partners

- Royal Prince Alfred Hospital
- Sydney Research

Charles Perkins Centre,
The University of Sydney

ABN 41 003 209 952

445 collaborations over 18 countries

HRI® IN 2020

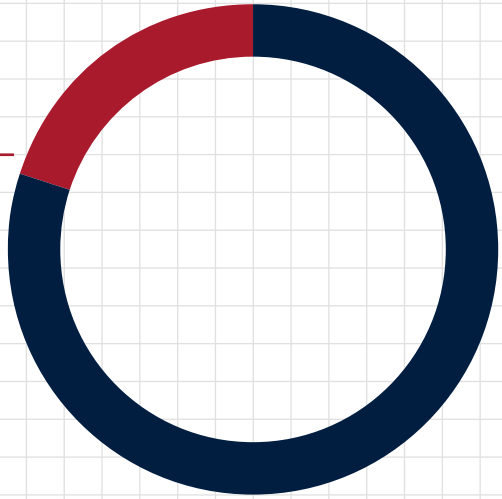
2020 HRI Income

TOTAL INCOME

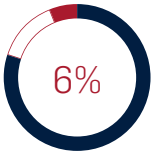
$20,111,301

Grants:
$3,932,847 (20%)

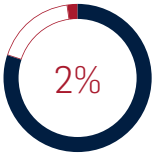
Fundraising (incl Bequests):
$16,178,454 (80%)



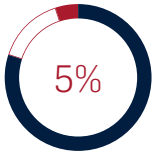
2020 grant income by funding body



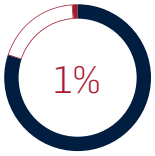
National Health & Medical Research Council
$1,159,786



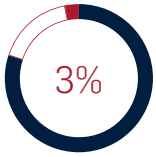
Universities
$470,254



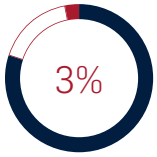
NSW Department of Health
$993,972



National Heart Foundation
$111,300



Research Block Grants
$690,466



Other
$507,069

STUDENTS TRAINED OR MENTORED

Honours	15
Visiting Honours	03
Masters	01
PhD	10
Visiting PhD	02
Summer Scholars	15
Visiting Students	48
Work Experience	03

107 Citations by external world-wide researchers to work published by HRI researchers

76 Discoveries published in peer-reviewed journals

60 Scientific projects currently being undertaken

Chair's Report

Professor Len Kritharides
MBBS, PhD, FRACP, FCSANZ, FAHA, FESC, FACC
Chair

Queen Elizabeth II famously commented on 1992 as being her "annus horribilis". For most of the world, 2020 was our annus horribilis. Over 105 million cases and over 2.4 million deaths from COVID-19 were recorded in a little over 13 months. Millions more uncounted infections, and millions more deaths from the undertreatment of non-COVID-19-related medical conditions are likely. Health care systems around the world have been placed under unimaginable pressure. The economic fallout of the pandemic has been extreme, even in Australia where we have been spared the worst of the pandemic.
For those of us involved in health care delivery, the acute re-organisation of services, realignment of normal processes of governance, and the hour by hour review of international and national information and government directives was perhaps analogous to a wartime footing. This was draining, exhausting, but ultimately, rewarding, because of the sense of unity, achievement and common purpose.

Why have Australia and New Zealand done so remarkably well? The good fortune to suffer from the "tyranny of distance" is one reason, allowing us the time to gather our thoughts and plan. The early realisation of the need for effective quarantine for overseas travellers was also a fundamental contributor. But to my mind, the most important factor was the co-operative interaction between Science and Government. Epidemiological science informed government policy on extensive contact tracing, on the need for lockdown, the need to wear masks, the aspiration to "flatten the curve" – overnight we became a country of armchair epidemiologists! Basic and translational science provided access to testing kits and to various types of vaccines, which we are now in the process of rolling out to our whole community. Cross-disciplinary science revealed the extent to which COVID-19 is much more than a lung disease, affecting most organ systems including heart, brain, kidneys and coagulation systems. But most of all, the mutual respect of government for scientific method, and the respect of scientists and clinicians for the need for good government responses, was fundamental. The achievements of our Sydney Local Health District (SLHD) led by Dr Teresa Anderson, and the Royal Prince Alfred Hospital (RPAH) virtual service, in particular, in delivering a remote access patient quarantine care service that permitted NSW hospitals to carry on their work as usual should be lauded as exemplars of the effective linkage between science, government and health care delivery.

For HRI, the COVID lockdown required closure of its laboratories at the Charles Perkins Centre, The University of Sydney. Many of our staff voluntarily reduced their working hours (and salary), and many moved into our Eliza St building. An enormous reorganisation of scientists and spaces at Eliza St was required to accommodate these changes. All was undertaken consistent with COVID-19 regulations, and included exhaustive testing and retesting for COVID-19 of all staff, using kits generously provided by Eliza St tenants Genetic Signatures. To our staff who voluntarily reduced their hours, to all our scientists and management team who managed to keep our research effort going because of these exceptional efforts, thank you.

Our staff cultural survey completed in 2020 by independent consultancy firm Voice Project yielded extraordinary results, with HRI achieving the status of Best Workplace in 2020 for providing an exceptional work environment for staff. What remarkable staff we have working with us at HRI. Read more about this award on page 40.

Fundraising is an important component of the viability of any research organisation. HRI has had a 30-year history of working closely with its donor community, who have supported our work unflinchingly.

The mutual respect of government for scientific method, and the respect of scientists and clinicians for the need for good government responses, was fundamental.

This year, with so many livelihoods upturned by the economic fallout from COVID-19, our donors continued their extraordinary support, a testament to the relationships our fundraising team, led by Richard Wylie, have developed with our donors over many years. Richard leaves us as Fundraising Director in 2021, and we thank him for his seven years of exemplary service to HRI. We look forward to his engagement with HRI in other capacities in the years ahead.

HRI scientists and clinician scientists were awarded $5.4M in NSW Health Cardiovascular Research Capacity Program grants from the Office of Health and Medical Research in 2020 – Professors Shaun Jackson, Angela Makris and David Celermajer, Associate Professors Simone Schoenwaelder and Sanjay Patel, and Drs Freda Passam, Paul Coleman and Lining (Arnold) Ju. Dr John O'Sullivan was awarded a prestigious five-year Heart Foundation Future Leader Fellowship, and Dr Ju from the Faculty of Engineering, The University of Sydney and HRI was awarded an NHMRC Ideas Grant. Read more about HRI's other grant success on page 42. The commercialisation pipeline at HRI continues to grow in size and diversity. We thank Sandra Boswell, who chaired this committee for us until October 2020, and welcomed HRI Governor John Batistich to the role of Chair of this important committee in November 2020.

HRI has worked closely with the SLHD, the Centenary Institute, the Woolcock Institute and The University of Sydney to support the case for the NSW Government funding a state-of-the-art research facility linked to the planned redevelopment of RPAH – the Sydney Biomedical Accelerator. The announcement of $750M NSW State Government funding for RPAH is a once-in-a-generational opportunity to develop linkages between discovery science and clinical care. A great deal of work has gone into refining strategic and governance concepts required for this project. As we await responses from the NSW Government for the latest submission, I would like to thank those Board members who made major contributions to this work on behalf of the HRI – specifically, Rod Halstead, Bruce Baird and Shaun Jackson, together with Tony Pollitt and Stephen Hollings.

A cup half empty or a cup half full? Given the year just gone, our good health, and the prospects of post-COVID recovery, I am firmly in the latter camp. Let us be thankful for all we have and all we have achieved, and look forward to a strong and expansive 2021 for HRI and you, its supporters.

Director of Cardiovascular Research Report

Professor Shaun Jackson
MBBS (Hons), BMedSci (Hons), PhD
Director of Cardiovascular Research

It's my pleasure to provide you with an update of the activities and achievements of HRI in what was a tumultuous 2020.

Medical research (at the best of times) is an immensely challenging undertaking. The difficulty in operating at the leading edge of human knowledge and the pressure to publish discoveries regularly in the world's leading scientific journals, matched to the highly competitive nature of the peer-reviewed grants system, means there are rarely many 'easy days' – which made 2020 astonishingly challenging for our researchers due to the COVID-19 pandemic.

Arterial Inflammation and Redox Biology Group

However, I am pleased to report that the resilience of our researchers shone through in 2020, as they kept their research moving forward, even while working remotely, home schooling their children, attending conferences virtually, and adapting to a series of 'COVID-safe' practices in the community and within our facilities.

During the COVID-19 pandemic, HRI proactively offered multiple employee wellbeing initiatives around mental health identification and management, upgraded virtual meeting solutions, as well as arranged for more company-wide online broadcasts to keep all staff across the Institute's changes, greater work flexibility, tools to reduce email volumes, and full transparency of COVID-safe planning.

In addition, HRI offered staff an in-house COVID-19 test using standard PCR assays. While not ratified diagnostic tests, these would still indicate if any staff were to be carrying the coronavirus. Staff were offered testing multiple times a week to minimise risk to the researchers on-site.

To check in on the wellness of our staff, we conducted a survey via the organisation The Voice Project. I'm pleased to report that our strong results secured HRI the 'Best Workplace Award 2020'. Read more about this award on page 42. This was a tremendous endorsement of the effort the HRI management team have invested in creating not just a performance-orientated culture, but also a culture that cares for our people in a personalised way.

Dr Christopher Stanley, Microvascular Research Unit Leader

While 2020 was a difficult year, it was also an exceptional year for scientific outputs.

Beyond the challenges of COVID, HRI welcomed two new research groups in 2020: the Arterial Inflammation and Redox Biology Group led by Professor Roland Stocker and the Microvascular Research Group led by Dr Christopher Stanley. It's something of a welcome back for Professor Stocker, who was one of the foundation Group Leaders at HRI's inception.

While 2020 was a difficult year, it was also an exceptional year for scientific outputs. Our researchers were rewarded for their hard work, winning numerous awards and funding grants, with Drs Lining (Arnold) Ju and Jessica Orchard both awarded multiple times in each category. Dr John O'Sullivan was also awarded a Future Leader Fellowship from the Heart Foundation and had multiple high-profile papers included in the highly prestigious *Nature Communications* journal, an achievement that saw his work featured on national TV. It's also worth highlighting that seven of HRI's researchers were awarded NSW Health Cardiovascular Research Capacity Program grants. Further details about these and other successes appear in Research and Media Highlights on pages 12–15 and in Notable Awards on page 42. A full listing of the papers published by HRI researchers and presentations can be downloaded here.

In closing, I would like to pay a special tribute to our operations and management teams led by Dr Stephen Hollings, who were able to stay one step ahead of the constantly evolving rules around COVID-19. Via their efforts, our organisation was able to stay COVID-free and functioning at a high level. A huge thank you also goes to our fundraising team led by Richard Wylie, who were able to adapt quickly to an environment where we couldn't hold live fundraising events, meet our donors face to face, or conduct tours of the Institute.

Finally, I'd like to thank the most special people of all – our valued donors. Without your generosity and belief in our cause, we simply wouldn't be able to make the breakthroughs that we do. Thank you.

Research and Media Highlights 2020

HRI researchers combat COVID-19

With the COVID-19 pandemic bringing the need for medical research to the forefront, HRI joined the fight by investigating the viability of pivoting development of its anti-clotting therapy for stroke to focus on combating the micro blood clots linked to severe COVID-19 cases.

This level of coverage is unprecedented in HRI's history and substantially raised HRI's profile on the global stage.

HRI also stepped up to raise awareness of the effects of COVID-19 on heart health, with Professor Shaun Jackson appearing on The Project (17 July 2020) to explain how COVID-19 can cause a blood-clotting disorder that affects all major organs in the body, leading to long-term damage.

HRI recorded over 140 pieces of media coverage for its COVID-19-related investigations, around the world and in Australia, on TV, in online and offline print media, and across the Australian radio network. This level of coverage is unprecedented in HRI's history and substantially raised HRI's profile on the global stage.

Television appearances included Professors Jackson and Ben Freedman on 7 News Sydney (17 June 2020), and Professor Freedman and Associate Professor Simone Schoenwaelder on the China Global Television Network (5 July 2020). Global news coverage included the worldwide newswires Reuters and Aljazeera, the Financial Post (US), Straits Times (Singapore), The Times (India), The Star (Malaysia), Daily Sabah (Turkey) and The Scottish Sun (UK). In Australia, many major titles ran stories, including the Australian Financial Review, The Sydney Morning Herald, Daily Telegraph, The West Australian, Australian Online, Courier Mail, The Advertiser, The Mercury and the Herald Sun, as well as numerous regional newspapers.
View full media report and video here.

Coronary Diseases publications

The Coronary Diseases Group, led by Associate Professor Sanjay Patel, published eleven papers in 2020, with collaborations including HRI's Clinical Research, Vascular Complications, and Atherosclerosis and Vascular Remodelling Groups.

Cardiovascular Neuroscience highlights

The Cardiovascular Neuroscience Group led by Dr Melissa Farnham, in collaboration with Drs John O'Sullivan and Kristina Cook (CPC), found that just six weeks of intermittent hypoxia dramatically alters energy metabolism in the heart and liver, with the heart showing alterations consistent with diabetes and heart failure. This study is ongoing, with one manuscript in preparation.

The Group also found that three weeks of a ketogenic diet may be a beneficial management strategy for protecting against the neurological consequences of severe hypoglycaemia without compromising the endogenous counterregulatory response. One manuscript has been submitted, with a second in preparation.

Why our hearts fail

Appeared on Channel 9 News and Sydney Morning Herald, 10 June 2020

Dr John O'Sullivan collaborated with Dr Sean Lal, director of the Sydney Heart Bank, the world's largest human heart bank, located at the Charles Perkins Centre, to examine cryo-preserved human hearts procured after transplantation. This resulted in several new heart failure discoveries that were published in the prestigious international journal *Nature Communications*.

The teams used advanced techniques to screen the heart tissue and measure thousands of proteins and other small molecules. Hearts with advanced heart failure were then compared with tissue from non-diseased hearts, matched for age, gender and BMI, for a deeper understanding of how they differ.

The researchers found changes in many important processes in the heart, including mechanisms that generate energy for the heart, mechanisms that deal with injury, clotting mechanisms, and processes that maintain structural integrity. The team will follow up many of their discoveries in the hope of finding new treatments. View full media report and video here.

Heart study debunks meat metabolite myth

Appeared on Channel 9 News, 16 April 2020

The Cardiometabolic Disease Group debunked the wildly publicised belief that the metabolite trimethylamine-N-oxide (TMAO) – linked to red meat and egg-rich diets – can clog up arteries, causing catastrophic heart problems like heart attacks and strokes. They discovered, contrary to other research, that TMAO is not responsible for common debilitating heart conditions. View full media report and video here.

Revealed: the molecule messing with your gym workout

Appeared on Channel 9 News, 16 May 2020

Research conducted by Dr Yen Chin Koay and the Cardiometabolic Disease Group revealed why some people fail to shed pounds and lower their cholesterol even when eating well and exercising hard. The research found that levels of a molecule called dimethylguanidino valeric acid (DMGV) appeared to indicate how much a person benefits physically from doing exercise. Those with higher DMGV do not reap the same rewards from working out hard and eating well as those with naturally lower levels of the metabolite. The work was published in the international journal *Cardiovascular Research*. View full media report and video here.

L-R: Dr Siân Cartland, Dr Mary Kavurma

The Vascular Complications Group, led by Dr Mary Kavurma, has shown that plasma TRAIL levels are reduced in patients with coronary artery disease, a significant finding.

Vascular Complications highlights

The Vascular Complications Group, led by Dr Mary Kavurma, has shown that plasma TRAIL levels are reduced in patients with coronary artery disease, a significant finding. This work was a collaboration with the Coronary Diseases and Atherosclerosis and Vascular Remodelling Groups at HRI as well as colleagues from the Westmead Institute for Medical Research, University of New South Wales, and Pontifical Catholic University of Chile. The findings were published in *Faseb Journal* and offer an alternate in silico approach for therapeutic target identification, such that finding new ways to elevate TRAIL levels in people to protect against diabetic vascular disease would be of therapeutic benefit.

The Group also published a manuscript in the *International Journal of Experimental Pathology* describing a fatty liver in hypertensive rats as well as a manuscript in *Redox Biology* in collaboration with colleagues from HRI and The University of Copenhagen. An invited review "TRAIL signals, extracellular matrix and vessel remodelling" was published in *Vascular Biology*, and another review on chemokines and stent biocompatibility was published in *Cardiovascular Research*. The latter was a collaborative venture with research colleagues from the South Australian Medical Research Institute.

Dr Kavurma was also interviewed by Female.com.au to raise awareness of diabetes, and by Women's Agenda to address some of the biases that occur for women in science, particularly in the fight for research funding.

Clinical Research highlights

The Clinical Research Group, led by Professor David Celermajer, published an important new work on heart disease in women – especially the impact of cardiac risk factors in pregnancy – and on the outcomes of young adults with congenital heart diseases.

Vascular Immunology highlights

The work of the Vascular Immunology Group investigating aspirin for preventing preeclampsia has won three national science prizes, now including the Andrew Phippard Memorial Award for best scientific research oral presentation at the Society of Obstetric Medicine of Australia & New Zealand annual meeting. This work has led to a major focus of the Australian Pharmacy Guild in providing advice for women at high risk of preeclampsia.

Ringing a vital alarm

Appeared in the Herald Sun, 2 October 2020

Professor Ben Freedman's collaboration with The Royal Melbourne Hospital resulted in a world-first multi-centre international study (SPOT-AF) that found smartphone monitoring of patients with stroke is effective in detecting atrial fibrillation (AF). Professor Freedman pioneered the use of this new technology for AF detection. The study monitored more than 1,000 patients over a period of three years, with sites spanning Australia, Hong Kong and China. The outcomes of the research will likely change clinical guidelines. View full media report here.

L-R: Prof Shaun Jackson, Imala Alwis, Dr Jessica Maclean

Thrombosis highlights

Despite the challenges imposed by 2020, researchers of the Thrombosis Group continued to achieve recognition for their research activities. These included a 2020 NSW Young Tall Poppy Award, received by Dr Lining (Arnold) Ju and awarded by the Australian Institute of Policy and Science. Also in 2020, Jessica Maclean was awarded her doctorate for her important work developing a novel ischaemic stroke model, and Ashly Davies-Graham was awarded first class honours and a "Dean's List of Academic Excellence for 2020" award for her studies examining a novel role for red blood cells in microvascular obstruction. The Group was also successful in securing research funding, with Drs Ju and Yuping Yuan awarded an Ideas Grant from the NHMRC, and Professor Shaun Jackson and Associate Professor Simone Schoenwaelder each receiving Senior Researcher NSW Health Cardiovascular Research Capacity Program grants from the Department of Health.

Heart Rhythm and Stroke Prevention highlights

Professor Ben Freedman and Dr Nicole Lowres wrote an editorial on the need for guidelines specific to Indigenous population screening for atrial fibrillation (AF). The Group also published a paper on Indigenous screening using Indigenous health workers, in collaboration with the Poche Centre, showing that AF is detected at an earlier age in this demographic.

Dr Jessica Orchard completed her PhD and won numerous awards, while Dr Katrina Giskes received the NSW & ACT Dr Charlotte Hespe Research Award and appeared in the Western Advocate newspaper (25 November 2020) for her work in AF self-screening. Read more about these achievements on page 42.

The AF-SMART II study, focusing on AF screening in rural areas, was completed and presented internationally and at the Cardiac Society of Australia & New Zealand conference, where it won the Prevention Prize.

The SPOT-AF study was completed, showing that stroke unit nurses could effectively screen for post-stroke AF with a higher detection rate than usual management with the Holter monitor. This will likely lead to incorporation in national and international guidelines.

Novel technology tools for self-screening of AF were developed and implemented in three practices, overcoming the challenges presented by the COVID-19 pandemic. The technology integrates three separate systems and has now been shown to be feasible.

Haematology Research highlights

The Haematology Group, led by Dr Freda Passam, published a paper in the journal *Diagnostics* evaluating the application of a fixed-endothelial whole-blood microfluidic model for the study of neutrophil involvement in thromboinflammation. The characteristics of their model provide the potential for further development for drug screening and point-of-care applications.

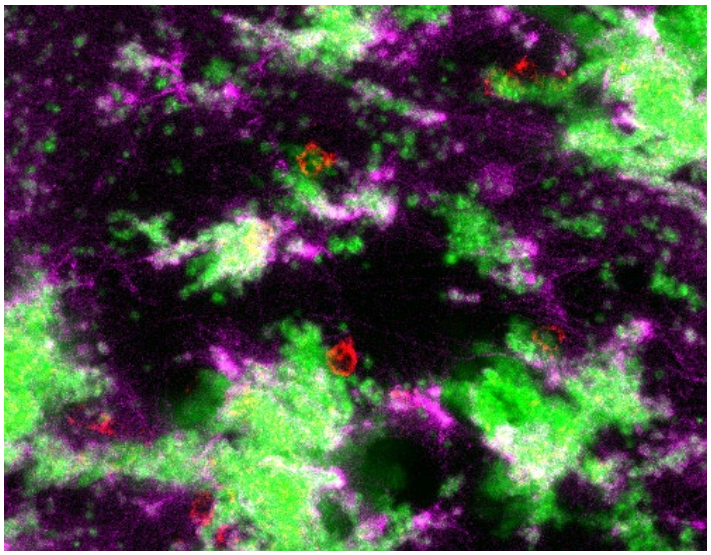


Image of thromboinflammation chip. Fibrin (magenta), platelet (green) and neutrophil (red) adhesion on endothelialized channel after perfusion of blood. Scale bar represents 20 µm.

Dr Ashish Misra
PhD, MTech, BSc
Unit Leader

Atherosclerosis and Vascular Remodelling Group

OUR MISSION

Our mission is to identify and gain insights from the genetic and molecular pathways involved in atherosclerotic disease in which the build-up of plaque in blood vessels causes thrombotic events including heart attacks. We aim to exploit these pathways to improve therapies with the aim of eradicating atherosclerotic diseases.

Our main objective is to broaden understanding of the cellular and molecular mechanisms involved in blood vessel wall patterning and define the role of these pathways in vascular abnormalities and complications. We continue to link these insights into translational research to prevent and treat atherosclerosis in humans.

To this end, we employ a unique blending of exclusive models and cultured cells, as well as human samples, with the aim of unveiling the pathogenesis of atherosclerosis.

Our ultimate goal is to prevent and reverse certain vascular diseases to prevent heart attacks and strokes.

Our ultimate goal is to prevent and reverse certain vascular diseases to prevent heart attacks and strokes.

Atherosclerosis and Vascular Remodelling team

Dr Ashish Misra

OUR IMPACT

Atherosclerotic cardiovascular disease is the leading cause of death globally, accounting for approximately one third of all deaths. Currently available therapies are not universally effective and do not reverse vascular disease completely, resulting in premature deaths and reduced quality of life for disease sufferers. With the need for continued treatment, there is a large burden on the health care system. Our work to identify the factors and signalling mechanisms involved in cardiovascular disorders has the potential to improve treatment options and eradicate atherosclerotic disease, thus increasing life spans and decreasing its burden on society.

RESEARCH PROJECTS

The role of Notch signalling in cardiovascular disease and related pathologies

Notch has been comprehensively studied as a conciliator of cell-to-cell communication that mediates cell fate decisions of progenitors. While Notch signalling has been extensively studied in cell fate determination at distinct development stages of mammalian cells and cancer stem cell progenitor maintenance and renewal, the functional role in vascular wall patterning and cardiovascular disease is not well understood. By using advanced microscopic techniques, fate mapping approaches and single cell clonal analysis, we aim to study the role of Notch signalling in blood vessel wall patterning and maintenance of smooth muscle cell progenitors in developing walls as well as disease of the vasculatures. Thus, we believe that the investigation of Notch signalling in vascular biology promises to be a fruitful way forward to designing new therapeutics.

Factors and regulators of smooth muscle cells and macrophages in progression of atherosclerosis

Atherosclerotic plaque consists of smooth muscle cells (SMCs) and macrophages in the malefactor lesion and are comprised of a lipid-laden core covered by a fibrous cap. Plaque rapture, due to weak caps, leads to thrombosis with dire consequences such as myocardial infarction and stroke. SMCs and macrophages are key players in this process. Although extensive research has been done in the past on atherosclerosis, exactly how cells from the normal blood vessel wall contribute to the atherosclerotic plaque cap is still far from clear. Our studies aim to discover the origin of the cells that form healthy blood vessels, how these cells contribute to plaque formation, and how these plaque cells can be manipulated to advantageously stabilise plaques to prevent rupture.

Modulating coronary atherosclerosis through perivascular fat (PVAT)

Organ-to-organ communications are vital for living systems and play critical roles in cellular homeostasis. Perivascular adipose tissue (PVAT) anatomically proximal to vasculature has a distinctive cellular composition that modulates a range of cardiovascular disease processes. We have previously shown that low dose colchicine therapy in patients with coronary disease significantly reduced inflammatory trans-coronary cytokine levels. As such, we hypothesise that colchicine pre-treatment prior to cardiac surgery will reduce diffusion of inflammatory cytokines from the vessel wall, thereby inhibiting differentiation of pre-adipocytes into mature adipocytes. Ultimately, this novel project will uncover how biological processes observed in one tissue (eg, PVAT) may influence key processes observed in a different tissue (eg, blood vessel). In turn, understanding these inter-organ communications will increase our understanding of pathways in cardiovascular disease, and hence provide new avenues to explore with existing and new therapeutics. Read more about this project here.

Find out more: www.hri.org.au/our-research/atherosclerosis-and-vascular-remodelling

Cardiometabolic Disease Group

Dr John O'Sullivan
MD, PhD, MSc, Cert Biostatistics (Harvard), FRACP, FAHA, FRCPI
Group Leader

OUR MISSION

Our mission is to improve the detection and treatment of cardiovascular disease through the development of diagnostic markers, predictors and novel therapies for cardiometabolic disorders.

We aim to discover new mechanisms in cardiometabolic disease that we can target with novel therapeutic agents. We also aim to detect early markers of disease to guide timely intervention. Our research revolves around two major themes: (i) uncovering mechanisms and identifying novel therapeutic targets in Heart Failure preserved Ejection Fraction (HFpEF); and (ii) diet-microbiome-metabolism interactions in cardiovascular disease.

OUR IMPACT

Cardiometabolic diseases, which lead to heart attacks and stroke, have exploded in prevalence due to a 600 per cent increase in overweight and obesity rates over the last 40 years. Our work to enable earlier detection of cardiometabolic disorders, and thus enable earlier intervention, could have a transformative impact on the health of hundreds of millions of people around Australia and the world who are at risk of diabetes and cardiovascular disease.

In our first theme, we have developed comprehensive resources with which to make novel insights: our own diabetic cardiomyopathy clinic; cardiac MRI; metabolomics and genomics platforms; in vivo murine models; an ex vivo perfusion Langendorff model; iPSC-cardiomyocytes, including several lines carrying loss-or gain-of-function variants in metabolic pathways relevant for cardiovascular disease; and stable-isotope flux analysis.

This work was recently supported by a National Heart Foundation Future Leader Fellowship. More recently, we have identified depletion of a molecule in human HFpEF hearts that is specific to this disorder and not seen in other types of human heart failure. We have replicated this result in a model of HFpEF, and demonstrated that replenishment of this factor can rescue HFpEF in this model. Now, we will begin a clinical trial to determine if replenishment of this molecule in human HFpEF hearts can also rescue HFpEF in patients.

In our second theme, we use matched diets, microbiome analysis, faecal and plasma metabolomics, and careful cardiovascular phenotyping, and have already identified several novel pathways.

Our work to enable earlier detection of cardiometabolic disorders, and thus enable earlier intervention, could have a transformative impact on the health of hundreds of millions of people around Australia and the world who are at risk of diabetes and cardiovascular disease.

RESEARCH PROJECTS

Leveraging cardiac substrates to improve cardiac energetics and outcomes in HFpEF
The "stiff" type of heart failure, where the heart cannot relax properly, has become the most common type of heart failure. While a range of therapies has been developed for the better-understood impaired-squeeze type of heart failure, shockingly there are no therapies for the stiff, impaired-relaxation type of heart failure, which is called Heart Failure preserved Ejection Fraction (HFpEF).

Recently, we have identified key pathogenic changes in human and model system HFpEF left ventricular myocardium and have also identified therapeutic strategies based on each of these discoveries.

We perform investigation of human heart tissue in conjunction with Dr Sean Lal from Sydney Heart Bank (over 17,000 samples, one of the largest in the world). We run a dedicated HFpEF clinic in our hospital, in which we use cardiac MRI to carefully characterise key features of HFpEF including extracellular volume, microvascular disease and fibrosis.

The Group has extensive tools to probe mechanisms including, in conjunction with HRI's Dr Xuyu Liu, drug modification technology to enhance therapeutic effectiveness. We also perform primary cardiomyocyte culture isolation from our human HFpEF myocardial tissue and our murine HFpEF myocardium to further probe mechanism. Read more about this project here.

Dietary-microbiome-metabolic interactions in cardiovascular disease
We are studying the interaction of dietary macronutrients with the microbiome, gut and plasma metabolome on cardiac phenotypic expression. Recently, we discovered a profound effect of high dietary fibre (resistant starch) diets on microbial profile and the plasma redox system, energetics, gut-derived vitamins, citric acid cycle metabolites, and a potent effect on tryptophan metabolism that confers anti-inflammatory effects. We are investigating further a tryptophan derivative that is produced exclusively in the gut and seems to have important roles in inflammatory-driven diseases like atherosclerosis and insulin resistance.

A key metabolic switch in cardiometabolic disease
Non-alcoholic fatty liver disease (NAFLD) is now the most common form of liver disease in the Western world. We recently discovered a new plasma biomarker (dimethylguanidino valeric acid [DMGV]) of liver fat that independently predicted diabetes up to 12.8 years before diagnosis in three distinct human cohorts of different ethnicity (O'Sullivan et al., J Clin Invest, 2017).
We have subsequently shown that DMGV is a "lifestyle" molecule, and predicts who will and will not respond to exercise intervention to modify their cardiovascular risk. We have delineated the dietary factors that alter its blood levels. It is also a marker of future coronary artery disease in patients independent of other risk factors. Future work will determine if modulating the generative pathway can modulate metabolic and cardiovascular risk. Read more about this project here.

Find out more: www.hri.org.au/our-research/cardiometabolic-disease

Cardiovascular Medical Devices Group

Dr Anna Waterhouse
PhD, BSc (Hons I)
Group Leader

OUR MISSION

Our mission is to understand the interaction of medical devices with patients' blood, proteins and cells, with a view to develop more sophisticated and compatible materials for medical devices.

We focus on how medical devices – such as artificial hearts, stents and bypass machines – interact with the body. The team applies cutting-edge bioengineering tools to develop new techniques to assess and understand the interplay of events at the biointerface and manipulate this interplay to improve medical device function as well as create novel devices, diagnostics and drug and non-drug-based avenues for therapies.

Our goal is to develop materials that reduce foreign reactions in the body, and to reduce the incidence of blood clot formation and biofouling.

OUR IMPACT

Despite the widespread use of medical devices in cardiovascular medicine, many side effects, such as blood clots (thrombosis) and microbe adhesion (biofouling), are promoted by the materials used to make these devices. Thrombosis of medical devices is currently managed with medication that can cause additional complications, such as bleeding from antiplatelet or anticoagulant drugs.

Additionally, biofouling is treated with antibiotics; however, antibiotics cannot always penetrate the biofilm and the overuse of antibiotics is leading to antibiotic-resistant pathogens. Increased understanding of biointerface interactions and methodology to assess materials could lead to the development of new, more compatible materials and devices to reduce the use of drugs, improve diagnostics for early disease detection and reduce risks for patients.

We focus on how medical devices – such as artificial hearts, stents and bypass machines – interact with the body.

RESEARCH PROJECTS

Biointerfaces

Understanding the interactions of medical devices with patients' blood, proteins and cells will allow the development of more sophisticated and compatible materials for medical devices for the diagnosis and treatment of cardiovascular disease. To achieve these goals, we utilise cutting-edge bioengineering tools to develop new methodologies to assess and understand the interplay of events at the biointerface. Read more about this project here.

Biomimetic model systems

Advances in material fabrication techniques and 3D printing in micro and nanotechnology have revolutionised bioengineering, allowing high precision manipulation of materials for modelling medical systems and devices in the lab. Using these strategies, biomimetic in vitro model systems can be generated to recreate physiological conditions to evaluate medical device materials, geometries and drugs. Device failure mechanisms and how different disease states contribute to them can be investigated with the aim of developing new treatments or preventative therapies.

Creating micro-systems to study medical devices and their failure mechanisms

Utilising the new facilities at The University of Sydney Nano Institute, this multidisciplinary project aims to create microsystems that mimic aspects of medical device materials and geometries. Using these microsystems, we will study how variations in material properties and blood flow dynamics govern the initiation of biomaterial-induced thrombosis. This knowledge can ultimately be used to improve or generate new materials for use in medical devices to improve their function and patient outcomes. Read more about this project here.

Bioengineering smart materials

Medical device thrombosis and biofouling leading to sepsis cause significant morbidity and mortality worldwide. Furthermore, there is an urgent need to reduce the complications that arise from drugs designed to combat these issues. Using bioengineering strategies, increasingly sophisticated materials can be constructed. By combining physical, chemical and biological surface modification methods, medical devices can be manipulated to interact with, repel or adhere proteins or cells to improve medical device function, create novel diagnostics and medical devices, and both drug and non-drug-based avenues for therapies.

Nanorobotics

Molecular-level changes in early heart disease occur on the nanoscale, and current diagnostic methods are inadequate for early detection. Bio-inspired by immune cells, we have established a multidisciplinary team from HRI, science, medicine and engineering to build synthetic nanorobots that move around the body to find and identify early-stage diseased blood vessels.

In this project, we will focus on designing and developing haematological and immunological compatible biomolecular devices by integrating molecular, protein and materials engineering. Read more about this project here.

Cardiovascular Medical Devices team

Slippery surface coatings to prevent thrombosis and pathogenic biofouling of medical devices

Newly developed, super slippery, liquid-repellent surface coatings have great potential to revolutionise medical devices, imparting anti-adhesive properties to materials.

Surface adhesion of proteins and cells is the driving factor in medical device fouling in processes such as thrombosis and pathogen adhesion in biofilm formation. We aim to clarify the mechanism by which the liquid-surface, Tethered-Liquid Perfluorocarbon (TLP), is anti-adhesive to proteins, mammalian cells and bacteria, with the goal of translating this to medical devices in the clinic to prevent their failure. Read more about this project here.

Find out more: www.hri.org.au/our-research/cardiovascular-medical-devices

There is much to be proud of, and much more to do if we are to provide the clarity of vision needed to combat cardiovascular disease. We are indebted to our resolute supporters and donors who have entrusted us to take this journey.

Professor Len Kritharides

Image: Laura Currie, Atherosclerosis and Vascular Remodelling Group

Cardiovascular Neuroscience Group

Dr Melissa Farnham
PhD, BSc (Hons I)
Unit Leader

Dr Melissa Farnham

OUR MISSION

Our focus is on how the brain controls breathing and blood pressure. We are interested in what goes wrong in the brain to result in the development of cardiovascular disease. We study peptides and their receptors in cardiovascular, autonomic, centres of the brain. Our current research aims to understand the central mechanisms driving the sympathetically mediated increases in blood glucose and blood pressure in models of sleep apnoea. By understanding the mechanisms driving the cardiovascular consequences of sleep apnoea, we aim to identify new therapeutic targets to treat sufferers and reduce disease burden.

OUR IMPACT

Cardiovascular disease (CVD) remains the leading cause of death in Australia and worldwide. It is often present with other confounding conditions such as obesity or obstructive sleep apnoea (OSA), both of which are independent risk factors for CVD.

The global burden of OSA is recently estimated as approximately 1 billion people and is comorbid in 30–80 per cent of cardiovascular (particularly hypertension) conditions and in approximately 70 per cent of diabetics. The associated Australian healthcare and economic costs due to comorbid disease and lost productivity are over $5 billion per year and are largely attributed to undiagnosed OSA. In conditions such as OSA, excess sympathetic activity may trigger development of cardiometabolic diseases, but research and concrete evidence is lacking.

We aim to significantly advance this research area. Our unique models and techniques are designed to uncover a previously unexplored mechanism that suggests OSA induces autonomic plasticity, which is important in the pathogenesis of CVD.

Results have the potential to dramatically expand our knowledge into the effects of intermittent stimulation and the capacity for plasticity to occur in primitive, life-sustaining areas of the brain.

RESEARCH PROJECTS

The autonomic consequences of sleep apnoea: a critical role for neuropeptides

OSA is characterised by repetitive pharyngeal collapse during sleep, with resultant oxygen desaturation (intermittent hypoxia) and sleep fragmentation. Metabolic effects of intermittent hypoxia occur rapidly. These early changes could initiate triggers that promote insulin resistance and development of type 2 diabetes in human OSA conditions.

Importantly, an excitatory neuropeptide and its receptors are present in areas of the brain activated by hypoxia; these areas control both blood pressure and blood glucose. In humans, genetic variations in this neuropeptide or its receptors are linked to sleep and metabolic disorders. Our focus is on how intermittent stimulation of brain circuits regulate blood glucose and blood pressure.

We recently showed that this neuropeptide is necessary in the brainstem for the sympathetic response to acute intermittent hypoxia. Our exciting new data indicates that the characteristic sympathoexcitation of OSA, that is likely to cause most of the subsequent pathological metabolic changes, is mediated by intermittent release of small amounts of this neuropeptide that act on receptors located on sympathetic neurons in the spinal cord.

Low carbohydrate (ketogenic) diet in type 1 diabetes: do ketones protect the brain from adverse effects of hypoglycaemia?

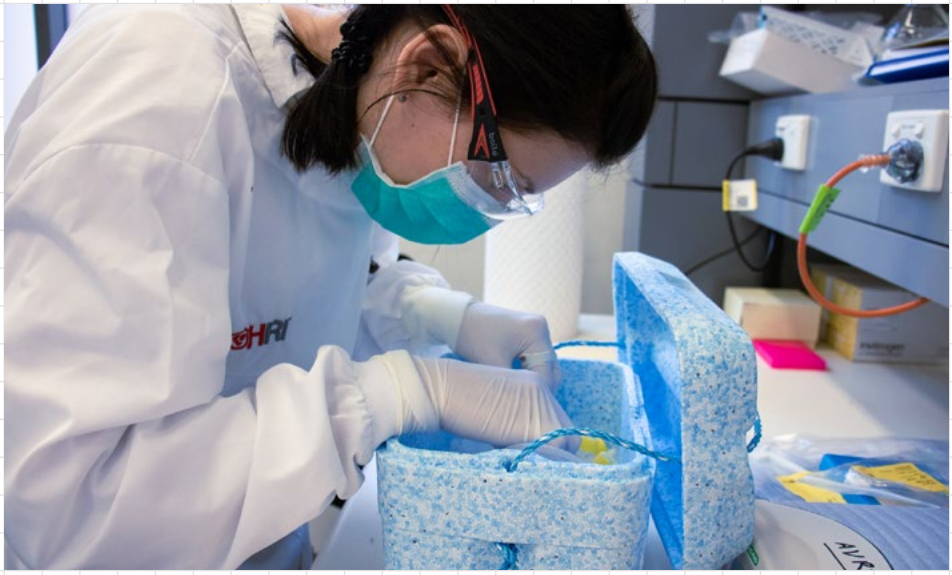
Type 1 diabetes accounts for 10–15 per cent of Australian diabetic patients. Type 1 diabetic patients are prone to repeatedly experiencing low blood sugar levels (hypoglycaemia), which results in a condition called hypoglycaemia unawareness. This condition, termed 'hypoglycaemia-associated autonomic failure' (HAAF), is life-threatening for type 1 diabetic patients.

Glucose is the major energy source for the brain under normal physiological conditions. However, during extended fasting, following exercise, or while on a high fat/low carbohydrate (ketogenic) diet, an alternative source of energy becomes available – ketone bodies. Although ketones are effective in the preservation of brain cognitive functions under hypoglycaemic conditions in type 1 diabetic patients, the effects of ketones on brain reflex response to recurrent hypoglycaemia and the development of HAAF in this patient population are unknown.

The aim of this project is to investigate the low carbohydrate ketogenic diet as a potential strategy in preventing the detrimental consequences of insulin-induced hypoglycaemia and the development of HAAF in type 1 diabetes.

Find out more: www.hri.org.au/our-research/cardiovascular-neuroscience

Results have the potential to dramatically expand our knowledge into the effects of intermittent stimulation and the capacity for plasticity to occur in primitive, life-sustaining areas of the brain.



Dr Polina Nedoboy

Dr Xuyu Liu
PhD, MSc, BSc
Unit Leader

Cardiovascular-protective Signalling and Drug Discovery Group

OUR MISSION

Our mission is to better understand the therapeutic mechanisms of cardiovascular-protective natural supplements in platelets and the heart, and use this knowledge to develop next-generation precision medicine for the prevention and treatment of life-threatening thrombosis and ischaemic stroke.

Recently, there has been considerable interest in the development of natural supplements for cardiovascular-protective therapeutics, due to their inherent safety profiles and the clinical evidence for ameliorating chemotherapy-induced cardiovascular complications. However, it remains a huge challenge to understand the cardiovascular-protective mechanisms at the molecular level, which impedes pharmacological optimisation of these bioactive agents for therapeutic use.

Our research aims to determine the protective mechanisms underlying heart-healthy diets and herbs, and apply this knowledge to design and develop safer and more effective cardiovascular therapeutics.

To this end, we focus on the development of new proteomic platforms to enable genome-wide understanding of how natural supplements and drugs perform in the context of cardiovascular complications, and on constructing a comprehensive chemical-proteomics database to reveal the therapeutic impacts on thrombosis at the cellular and molecular level.

We also focus on adopting new drug discovery technologies – PROTAC and ABPP that have led to a tremendous achievement in anti-cancer drug discovery – to accelerate the development of precision medicine to tackle thrombosis and ischaemic stroke. In particular, leukocytes, ie, neutrophil and macrophage, have been strongly implicated in the pathogenesis of thrombosis. We aim to develop new PROTAC molecules to tackle the challenge of severe thromboinflammation that leads to the poor prognosis of cardiovascular disease and COVID-19.

Our research aims to determine the protective mechanisms underlying heart-healthy diets and herbs, and apply this knowledge to design and develop safer and more effective cardiovascular therapeutics.

OUR IMPACT

Thrombotic complication is the leading cause of mortality and accounts for one in four deaths worldwide. Despite intense investigation over the past decades, the discovery of novel cardiovascular drugs has remained disappointingly low. Novel antithrombotic drugs entering clinical testing have stalled due to the large attrition in investment and increasing demand in risk assessment. However, the existing antithrombotic drugs such as aspirin and clopidogrel are ineffective, with less than 15 per cent of diabetic patients taking these medicines avoiding a fatal thrombotic event. This situation is likely to worsen in the near future due to the rapidly growing incidence of obesity and diabetes.

The chemical biology research approach adopted by our group is designed to identify effective and durable antithrombotic therapy inspired by natural supplements, and to repurpose anti-cancer and anti-inflammatory drugs for thrombotic conditions.

RESEARCH PROJECTS

Understanding heart-healthy diets at the molecular level
Sulforaphane and alliin are known to be the cardioprotective "ingredients" in broccoli and onion diets. They have been shown to promote cardiomyocyte survival against ischaemic injury and exhibit potent anti-cancer activity by potentiating apoptosis. However, the protein target spectra of these small molecules in cells remain unclear. There is no unified model to explain the cell-type-dependent phenotypes observed in the treatment. This research is partially conducted in collaboration with the Payne research group (School of Chemistry, The University of Sydney).

Chemical synthesis and phenotypic validation of precision proteolysis targeted chimeras (PROTACs) for cancer and cardiovascular disease
Akt kinases have been associated with the development of thrombosis, cancer and other major killer diseases. This kinase family is composed of three highly homologous isoforms: Akt1, Akt2 and Akt3. Recently, the revolutionary approaches in drug development termed PROTAC (PROteolysis-TArgeting Chimera) have attracted considerable attention in repurposing broad-spectrum therapeutics to be target-selective degraders. This project aims to develop Akt-isoform-specific PROTACs and to investigate their therapeutic potential in thrombosis. We have recently established two Akt2-isoform-selective degraders and are in the process of optimisation and biological validation. Read more about this project here.

Towards the development of more effective and safer high-affinity ACE2 variants for the treatment of COVID-19
Infection by SARS-CoV-2 – the etiological virus underpinning the current COVID-19 pandemic – has been shown to lead to a substantial decrease in surface expression of the ACE2 receptor. Ultimately, this leads to a high tendency to trigger acute respiratory distress syndrome. To address these ongoing issues, we aim to develop high-affinity ACE2 variants that are capable of scavenging SARS-CoV-2 virus effectively in vivo while offering lung- and cardiovascular-protective effects to equivalent levels with respect to current recombinant ACE2 therapeutics. Read more about this project here.

Chemical knock-out of proteins in primary leukocytes using PROTAC-based modulators
In this project, we will design and create a conditional knock-out system that leverages the potency of PROTACs and photosensitive molecular probes, which will enable the investigation of transient protein functions in leukocytes and platelets responding to thrombotic cues. Read more about this project here.

Find out more: www.hri.org.au/our-research/cardiovascular-protective-signalling-and-drug-discovery

Clinical Research Group

Professor David Celermajer AO
MBBS, MSc, PhD, DSc, FAHA, FRACP, FAA
Group Leader

Early detection and prevention of advanced heart disease may save hundreds of thousands of lives each year.

OUR MISSION

Our primary mission is to detect cardiac and vascular disease promptly in order for treatments to be administered at an early, optimal stage to prevent serious late consequences of disease.

Our goals are to detect and prevent complications from three primary types of serious heart disease:

(i) atherosclerosis – the narrowing of the main blood vessels in the body, and the main cause of heart attack and stroke;

(ii) congenital heart disease – as an increasing number of adults surviving with inborn heart problems still require extensive care and treatment; and

(iii) pulmonary vascular disease – the narrowing of the main blood vessels to the lungs, which can lead to overload of the right side of the heart.

OUR IMPACT

Early detection and prevention of advanced heart disease may save hundreds of thousands of lives each year. We aim to detect heart and blood vessel abnormalities at an early stage before the condition becomes irreversible. We design interventions to treat a wide range of abnormalities, with a particular focus on the prevention of atherosclerosis in children and young adults who have risk factors for early heart disease, obesity, exposure to passive smoke in the home, those who smoke themselves, or those with high levels of cholesterol. We also concentrate on all subject ages with pre-diabetes or diabetes, and babies who are born small at full term.

RESEARCH PROJECTS

We have a series of projects to detect early blood vessel damage in children and young adults as well as programs to intervene to prevent late serious complications. We also study heart disease in those with congenital cardiac abnormalities with a view to minimising complications and maximising quality of life.

Detecting heart attacks
In collaboration with Associate Professor Sanjay Patel and the Coronary Diseases Group at HRI, we have discovered that the heart releases certain proteins and cell remnants during a disruption of plaques (during heart attacks), and we can now detect these in the laboratory. Dr Gonzalo Martinez, a cardiologist from Chile, helped perform this work, collaborating with our Group for 18 months. Read more about this project here.

Early detection of pulmonary vascular disease
Pulmonary vascular disease, or high blood pressure in the lungs, is a very severe condition affecting young adult Australians and (as we are increasingly finding out) older Australians also. We conducted two projects to outline novel techniques for detecting this complication before it caused more serious health problems. Read more about this project here.

Young adults with congenital heart disease
At the Royal Prince Alfred Hospital (RPAH), we run one of the largest Adult Congenital Heart Disease Clinics in the country. Our work with these young adults has focused on rarely studied conditions such as Ebstein's anomaly of the heart, congenitally corrected transposition of the great arteries and dextrocardia (the unusual situation where the heart lies on the right side of the chest rather than the left). We have also collaborated with the Department of Radiology at RPAH to make important discoveries about a condition called noncompaction of the heart. Read more about this project here.

Improving health outcomes in congenital heart disease for young adults, their families and the health system
Ninety per cent of children born with congenital heart disease (CHD) are surviving to adult life. Recently, the characteristics of this population have been changing, as advances in medical practice are allowing people with CHD to live longer. This project aims to acquire missing "life experience" and "health systems" knowledge, enabling further research that will drive new care strategies that will improve patient wellbeing and ease the burden on the health system. Read more about this project here.

This type of project has not been done elsewhere, and so has the potential to be a world first.

MEDICAL RESEARCH FUTURE FUND GRANTS

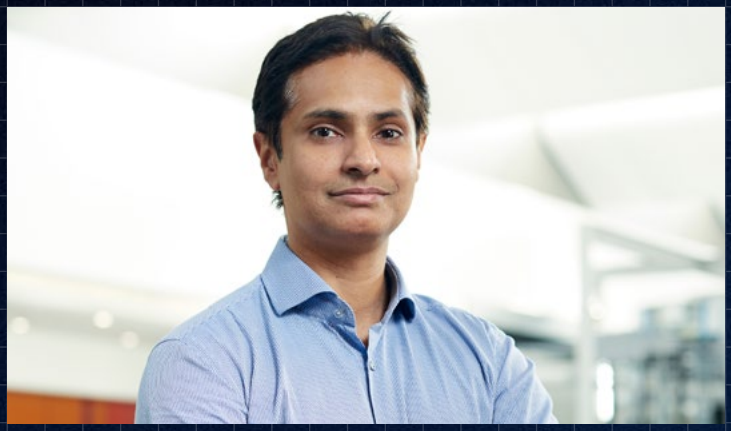
In 2020, we had terrific success with grant funding in this area, from the Medical Research Future Fund (MRFF) – both the two largest grants for the whole of Australia in the 2020 Heart Research Funding Round were made to our Group for the below project areas.

Optimising exercise prescription and delivery in congenital heart disease – The Congenital Heart Fitness Intervention Trial: CH-FIT
This project is designed to improve quality of life and exercise capacity for people living with CHD. HRI will undertake the first multi-centre randomised controlled exercise intervention in children and adults living with CHD employing a scalable model of care, integrating physical activity and behaviour change techniques. Read more about this project here.

Australian-wide study of the outcomes and burden of congenital heart disease across the life-course
This project is working to establish a unique National CHD Registry for 25,000 CHD Australians and develop it into a world-class resource with profound translational impact.Read more about this project here.

Find out more: www.hri.org.au/our-research/clinical-research

Coronary Diseases Group



Associate Professor Sanjay Patel

PhD, MBBS (Hons 1 Syd), FRACP, FCSANZ

Group Leader

OUR MISSION

Our mission is to reduce death and disability associated with heart disease by reducing atherosclerotic plaque build-up.

Our research aims to develop novel therapies to target atherosclerosis (arterial blockages) and its consequences (heart attack). Our treatment mission is to develop dedicated agents that specifically target the inflammation that drives coronary plaque instability. Our work is performed in collaboration with the Clinical Research, Vascular Complications and Atherosclerosis and Vascular Remodelling Groups within HRI, drawing upon their expertise in each area of research.

OUR IMPACT

One Australian dies from an acute coronary syndrome (ACS) every 51 minutes. Failure to specifically target persistent coronary inflammation, which drives high rates of recurrent events, is likely a major factor. To address this problem, our program's overarching aim is to: (i) elucidate new inflammatory pathways in ACS patients and (ii) re-purpose established anti-inflammatory drugs that target these pathways. We have focused on colchicine, a safe, cheap and effective anti-inflammatory agent.

Our program was the first to show that colchicine has striking athero-protective effects. Our findings are recognised internationally, with 20 papers and 25 presentations (at national and international scientific symposia) in the last five years. Notably, this program's work has been cited 202 times by groups in 16 countries (Google Scholar), demonstrating its reach.

RESEARCH PROJECTS

Effects of colchicine on clinical and imaging endpoints in patients post-acute coronary syndrome (ACS) and stroke
We recently showed that oral colchicine has striking anti-inflammatory and plaque-stabilising properties in ACS patients already on optimal medical therapy (OMT), including high dose statin. In particular, we found that in ACS patients, "single shot" colchicine markedly suppresses monocyte inflammasome activation and trans-coronary inflammatory cytokine levels (PMID: 26304941). Also, long-term oral colchicine therapy in patients post-ACS resulted in coronary plaque stabilisation and a concomitant reduction in plasma CRP concentrations (PMID: 29055633). We recently were awarded funding (from NHMRC, MRFF) to conduct multi-centre randomised control trials of colchicine in ACS (COLCARDIO-ACS) and stroke (CASPER) survivors, who have elevated biochemical markers suggestive of persistent coronary inflammation (hsCRP ≥3 mg/L). Importantly, these patients have the highest risk of recurrent MACE and are expected to derive most benefit from suppression of coronary inflammation. We will embed imaging endpoints into these studies, including coronary inflammation imaging to identify colchicine's effects on ruptured and high-risk coronary plaque and carotid plaque.

The effects of colchicine on the development and regression of atherosclerosis
This study aims to investigate colchicine's effects on both plaque development and regression. Utilising a well-established lab model of atherosclerosis, we are able to determine whether colchicine treatment can affect the contents of atherosclerotic plaque by modulating its cellular components and subsequently reducing overall plaque burden.

This study consists of two models: a treatment regression model, in which we will assess whether colchicine can reverse pre-formed plaque build-up, and a prevention model, in which we will assess whether colchicine can prevent plaque development.

Determining the effects of colchicine on smooth muscle cell plasticity in advanced atheroma
This collaborative study (with the Atherosclerosis and Vascular Remodelling Group at HRI) uses novel murine models of atherosclerosis to understand molecular athero-protective properties of colchicine.

Determining the anti-atherosclerotic properties of TRAIL
Through collaboration with HRI's Vascular Complications Group, we continue to study potential therapies to boost TRAIL, a novel mediator with marked anti-inflammatory and anti-atherosclerotic properties, in patients with coronary disease.

Find out more: www.hri.org.au/our-research/coronary-diseases

Haematology Research Group

Dr Freda Passam
MD, PhD, FRACP, FRCPA
Group Leader

Haematology Research team

OUR MISSION

Our mission is to discover new mechanisms of clot formation that can lead to the development of efficient and safer antithrombotic drugs.

We have a special interest in the development of biochips for the detection and monitoring of thrombotic tendency. We are focused on the role of enzymes, named thiol isomerases, in the development of thrombosis and their potential as novel antithrombotic targets. An exciting new project is to define the proteomic signature of the diabetic platelet to identify causes for increased thrombotic risk in patients with diabetes. In the clinical space, we are interested in the management of venous thrombosis in the community and high-risk thrombosis.

Our research goals are to: (i) discover new targets to prevent thrombotic complications in patients with diabetes; (ii) characterise thiol isomerase inhibitors as new antithrombotics; and (iii) develop new diagnostic tests to detect prothrombotic tendency in patients with cardiovascular risk factors.

OUR IMPACT

Current antithrombotic treatment is not effective or has bleeding side effects, eg, one in six patients who have had a heart attack will have another attack despite optimal treatment. We aim to find answers to fundamental biological problems that will enable the development of new diagnostics and treatments for patients with blood clots.

RESEARCH PROJECTS

Thiol isomerases as novel antithrombotic targets
Thiol isomerases are enzymes in the circulation that control the function of clotting receptors and proteins by reacting with their disulphide bonds. We have identified a novel clotting pathway that involves enzymes, named thiol isomerases. Inhibitors of these enzymes can be developed into drugs that treat thrombotic disease. The aim of this project is to dissect the role of thiol isomerases in thrombus formation using genetically modified mice, in vivo thrombosis models and thiol isomerase inhibitors.

Defining the diabetic "platelome"
Platelets are necessary to form blood clots to prevent bleeding. However, in patients with type 2 diabetes mellitus, platelets are more likely to form clots than normal. The aim of this project is to define the "platelome" (proteomic-metabolomic-lipidomic-transcriptomic phenotype) of platelets in patients with diabetes for the identification of biomarkers of thrombotic risk and new therapeutic targets

Biochips for the assessment of haemostasis and thrombosis
Many patients with bleeding and clotting disorders go undetected by routine laboratory tests because these do not reflect the conditions in the body's circulation. Our group uses biochips in a microfluidic system that simulates human circulation. These biochips can be used to detect a thrombotic or bleeding tendency in patient samples.

Find out more: www.hri.org.au/our-research/haematology-research

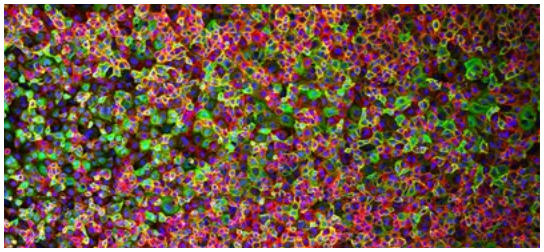
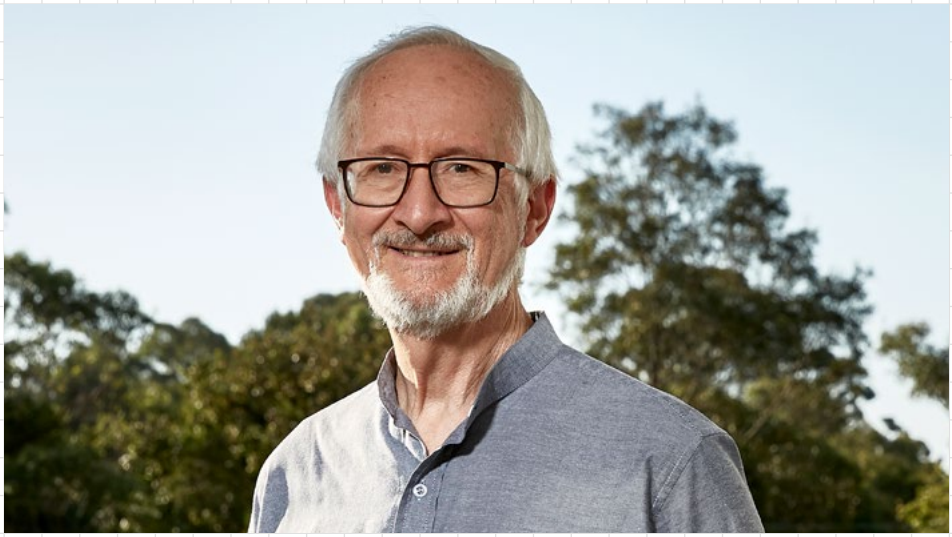


Image of endothelialized chip. Microfluidic channel coated with endothelial cells stained for actin (red), nuclei (blue), and intercellular adhesion molecule 1 (green). Scale bar represents 100 µm.

Heart Rhythm and Stroke Prevention Group



Professor Ben Freedman OAM

PhD, MBBS, FRACP, FCSANZ, FACC, FESC, FAHA

Group Leader

OUR MISSION

Our mission is to prevent strokes through early detection of silent atrial fibrillation (AF) and implement appropriate guideline-based management.

With a clinical implementation focus, we are exploring novel strategies using eHealth tools to detect unknown silent AF. AF is the most common abnormal heart rhythm – it is estimated that individuals over the age of 40 have a one in four lifetime risk of developing AF. AF is responsible for almost one third of all strokes, which are largely preventable by anticoagulant medications that stop clots from forming inside the heart. Unfortunately, AF is frequently silent, especially in older people who are at greater risk of stroke, with the first sign of AF being a severe stroke.

Our AF screening research extends through collaborations with primary care and specialist clinics in Australia, the USA, Shanghai, Hong Kong, Japan, Vietnam, Germany and the UK.

Another major interest of our Group is to determine whether our Indigenous population has a higher burden of AF by screening in remote and rural Australia, in collaboration with the Poche Centre and the University of Auckland, New Zealand.

OUR IMPACT

Our main activities are to determine how best to screen for AF at scale, and to prevent as many strokes as possible. The more people screened and treated, the more strokes we can prevent. We continue global advocacy for screening for AF through the AF-SCREEN International Collaboration. This is likely to change guidelines and influence future government policy and have a global impact on stroke reduction. In fact, the Australian Heart Foundation and Cardiac Society of Australia & New Zealand 2018 guideline on the management of AF had opportunistic screening for unknown AF as its first recommendation, with a practice point being about use of a handheld ECG pioneered by our Group, quoting our Group's work in its recommendation. Many of our papers on screening were also cited in the 2020 European Society of Cardiology AF guidelines.

We continue global advocacy for screening for atrial fibrillation through the AF-SCREEN International Collaboration. This is likely to change guidelines and influence future government policy and have a global impact on stroke reduction.

RESEARCH PROJECTS

- Atrial Fibrillation Screening, Management, and guideline-Recommended Therapy (AF-SMART) studies: in metropolitan and rural general practice using smartphone ECG and a suite of eHealth tools *(completed)*
- Patient self-screening for AF in general practice using screening stations *(ongoing)*
- Patient self-screening using a smartphone ECG to identify recurrence of postoperative AF after noncardiac surgery and medical admissions: in Concord Hospital, Royal Perth Hospital, and Gosford Hospital *(completed)*
- Analysis of time-trends of anticoagulant prescription for AF in general practice *(ongoing)*
- Assessment of general practitioner practices regarding AF management *(ongoing)*
- Collaboration with the Poche Centre to screen for AF in Indigenous Australians in remote and rural NSW, NT and WA *(completed with potential for future studies)*
- Collaboration with researchers in Royal Melbourne Hospital to detect AF post-stroke in Australia, Hong Kong and China (SPOT-AF) *(completed)*
- Collaboration with researchers at the Chinese University of Hong Kong to screen for AF in cardiac clinics, general practice and the community *(completed – over 20,000 people screened)*
- Collaboration with researchers in Shanghai (China) to screen for AF in community centres (AF-CATCH) *(completed)*
- Collaboration with researchers in Hanoi (Vietnam) to screen in hospital to detect AF after cardio-thoracic surgery *(completed)*
- Collaboration with Hamburg and Gutenberg Heart studies (Germany) on screening for AF *(completed)*
- Collaboration with researchers in Frankfurt (Germany) about epidemiology of AF *(ongoing)*
- Collaboration with researchers in Oklahoma (USA) to screen for AF in tribal Indian clinics *(completed)*
- Collaboration with researchers in Toyama (Japan) to investigate the incremental yield of annual screening *(completed)*
- Collaboration with researchers in Thailand screening in rural areas using village health workers *(completed)*
- Collaboration with researchers in Malaysia screening as part of an aging cohort study *(ongoing)*

Find out more: www.hri.org.au/our-research/heart-rhythm-stroke-prevention

Professor Shaun Jackson

MBBS (Hons), BMedSci (Hons), PhD
Group Leader

Thrombosis Group

OUR MISSION

Our mission is to establish new and innovative approaches to the prevention and treatment of heart disease and stroke, positioning Australia as a leader in the discovery and development of innovative therapies for the treatment of atherothrombotic diseases.

Our research is focused on the haemostatic and innate immune systems and their dysregulation in cardiovascular disease. Our main focus is on blood cells (platelets, leukocytes), blood coagulation proteases and endothelial cells.

While our studies are primarily aimed at defining new mechanisms underlying clot formation in healthy individuals and applying this knowledge to better understand mechanisms leading to platelet hyperactivity (thrombosis) and inflammation (termed thromboinflammation), our ultimate aim lies in the translation of our research discoveries into new therapeutic approaches to treat cardiovascular diseases, including heart attack, stroke, diabetes and the metabolic syndrome.

OUR IMPACT

Atherothrombosis is arguably Australia's greatest healthcare problem, affecting over 50 per cent of the adult population. Despite intense investigation over the last 40 years into the discovery and development of more effective antithrombotic drugs, the impact of these therapies on mortality rates has remained disappointingly low. This situation is likely to worsen in the future due to the rapidly growing incidence of obesity, diabetes and the metabolic syndrome – diseases that are typically more resistant to the benefits of "classical" antithrombotic therapy. The comprehensive research approach adopted by our Group is designed to identify and target thrombosis risk in such diseases.

RESEARCH PROJECTS

Understanding mechanisms leading to microvascular dysfunction and poor cerebral perfusion in stroke

For patients presenting with acute myocardial infarction or stroke, the primary goal of therapy is to promptly re-open blocked arteries (recanalization) to salvage the dying ischaemic tissue. A common complication of treatment is microvascular obstruction. Using cutting-edge techniques, we have observed previously unappreciated in vivo changes within the microvasculature during ischaemia reperfusion. Our findings not only demonstrate an intimate spatiotemporal relationship between endothelial injury and vaso-occlusion mechanisms, they also help explain why existing therapies remain ineffective. Read more about this project here.

Biomechanical sensing and blood clot formation: Solving a sticky clotting problem in diabetes
The leading cause of death in diabetes is cardiovascular disease, with up to 70 per cent of deaths relating to the development of blood clots supplying the heart (heart attack) or brain (ischaemic stroke). We have discovered a new biomechanical clotting mechanism severely affected by diabetes that is resistant to the beneficial effects of commonly used antithrombotic agents. Studies are also examining the role chronic oxidative stress plays in amplifying blood clotting in diabetes, and the mechanisms by which oxidative stress may modify platelet receptors to enhance adhesion.
Read more about this project here.

Thrombosis team

Developing novel approaches to the treatment of ischaemic stroke
The central goal of stroke therapy is the prompt reperfusion of occluded blood vessels to minimise tissue death, with administration of "thrombolysis" (intravenous recombinant tissue-type plasminogen activator, rtPA) – the only clinically approved drug available to stroke patients. Despite this, the use of rtPA is associated with significant side effects, limiting its widespread use. We are designing new scientific models (i) and working on several novel approaches (ii, iii) to improve upon existing stroke therapies, making them safer and more effective.

(i) Development of a novel preclinical ischaemic stroke model: Our ongoing studies have successfully developed a novel model of thrombolysis (iCAT) that for the first time allows us the ability to examine the efficacy of novel drugs including novel thrombin inhibitors to facilitate clot lysis (recanalization), restore perfusion in the brain, as well as determine whether cerebral damage and cognitive impairment associated with stroke are reduced. We are using this model to assess the efficacy of currently approved and novel anticlotting agents to facilitate stroke treatment.

(ii) Developing safer anti-clotting agents derived from "Mother Nature": In collaboration with Professor Richard Payne at The University of Sydney's School of Chemistry, we are characterising novel anticlotting agents that have been based around naturally occurring proteins found in saliva of blood-feeding insects, including mosquitos and ticks. Our initial studies have demonstrated these bug-derived proteins are able to dissolve blood clots in disease models of thrombosis with fewer bleeding complications, laying the foundation for the development of safe anticoagulants for the treatment of thromboembolic diseases such as stroke in the future. Read more about this project here.

(iii) Safety and Tolerability of a novel antiplatelet in patients with Acute Ischaemic Stroke (STARS): We have established a key group of collaborators comprised of Australian stroke clinicians and clinical trialists in the area of ischaemic stroke (Chris Levi (UNSW, Newcastle), Craig Anderson, Candice Delcourt (RPA, The George), Bruce Campbell (RMH), Ken Butcher (POW), Tim Ang (RPA)). Together we are drafting plans for a phase IIa multicentre, multinational, dose escalation study. The primary aim of this study is to evaluate the safety and tolerability of our novel antiplatelet as an adjunct therapy in patients with acute ischaemic stroke, when given in combination with current standard of care, and will be the basis for future phase IIb and III efficacy studies.

Platelet death as an important regulator of blood clot formation
Our studies have demonstrated that procoagulant platelets are dying cells, undergoing a cell death process akin to necrosis, leading to phosphatidylserine exposure and thrombin generation. We are continuing to characterise these pathways to determine their role in clot formation in health and disease. Read more about this project here.

Find out more: www.hri.org.au/our-research/thrombosis

Our ultimate aim lies in the translation of our research discoveries into new therapeutic approaches to treat cardiovascular diseases.

Vascular Complications Group

Dr Mary Kavurma
PhD, BSc (Hons)
Group Leader

OUR MISSION

Our mission is to understand the pathogenesis of blood vessel disease and its complications. Using this knowledge, we intend to identify novel strategies and therapeutics to reduce the burden of cardiovascular disease (CVD) on people.

Our research uses various models, genetic manipulation, and biochemical and molecular biology tools to dissect how blood vessels become dysregulated, with an emphasis on changes to gene expression, vascular cell adaptation and function in both normal and abnormal settings in the blood vessel wall.

OUR IMPACT

Our research aims to understand the molecular, biochemical, and cellular mechanisms underlying blood vessel diseases, focusing on atherosclerosis and its complications, including peripheral vascular disease and diabetes. By providing new insights on blood vessel dysregulation in CVD and related pathologies, our work will help uncover new strategies and therapeutics to combat disease, ultimately improving quality of life and life expectancy.

RESEARCH PROJECTS

Vascular calcification
Medial vascular calcification is increasingly recognised as a complication of aging in patients with CVD, such as atherosclerosis, as well as in diabetes mellitus and chronic kidney diseases. Importantly, medial calcification is associated with the morbidity and mortality of these patients. For the development of new and better therapeutics, understanding how calcification is regulated in blood vessels needs to be further investigated. This is an ongoing project that investigates how vascular smooth muscle cells control and promote vascular calcification.

The role of monocyte/macrophage dependent TRAIL signals in atherosclerosis
Atherosclerosis is an inflammatory condition and the primary cause of CVD, initiated by retention of cholesterol in the vessel wall, leading to the recruitment and differentiation of monocytes into macrophages. TRAIL (TNF-related apoptosis-inducing ligand) is produced by most cells in the body. Intriguingly, low TRAIL levels independently predict cardiovascular events and mortality, and circulating TRAIL levels are lowered in patients with CVD. Importantly, our murine models with TRAIL deletion have the same symptoms as CVD patients. Why TRAIL levels and expression are reduced with atherosclerosis are presently unknown. This project seeks to investigate the function of TRAIL, and how TRAIL's protective actions in atherosclerosis relate to its role in monocytes and macrophages, and whether increasing levels in these cells can improve disease.

Novel mechanisms regulating angiogenesis in disease
Diabetics are three to four times more likely to develop atherosclerotic coronary and peripheral artery disease, conditions where narrowed arteries reduce blood flow to the heart and limbs. This is a major risk factor for lower-limb amputation and increased risk of myocardial infarction. Current interventions are insufficient in many patients because extensive disease precludes effective revascularisation. One option is to stimulate blood vessel growth to restore blood flow, preserve tissue survival and maintain optimal organ function. This ongoing project seeks to identify novel molecules that stimulate stable blood vessel networks in the heart and limbs of diabetic and non-diabetic patients during ischaemia.

Find out more: www.hri.org.au/our-research/vascular-complications

Vascular Immunology Group

Distinguished Professor Annemarie Hennessy AM

PhD, MBBS, FRACP, MBA

Group Leader

OUR MISSION

Our mission is to better understand the causes of preeclampsia (high blood pressure in pregnancy), the condition's impact on women during pregnancy, and the impact on long-term cardiovascular health. We seek to develop new drug treatments for preeclampsia.

Our research focuses on how placentas work and the benefits of placental treatment to women that we look after in clinical practice. Professors Hennessy and Makris, and Drs Aggarwal, Chau, Rajkumar and Shanmugalingam are active physicians caring for hundreds of women annually with preeclampsia, hypertension, vascular and kidney diseases. Our research scientists, Drs Liu (since Oct 2019), Pears and Welsh, are experts in animal studies and in growing placentas, and thus support the projects of the Group. The Group is supported by the Sydney Local Health District (SLHD) and significant NHMRC project grant funding administered by Western Sydney University (WSU). The placenta and women's health research adds important and novel dimensions to the overall research plan at HRI. We have strong collaborations across Sydney, and internationally, and in 2020, with the Kolling Institute at Royal North Shore Hospital with The University of Sydney.

Our work is strongly driven by a women's action group, The PEARLS Group, who provide community engagement and review of research plans, as well as funding to support the Vascular Immunology Group's work. In 2020, The PEARLS Group raised over $55,000 for the Vascular Immunology Group for a PhD Scholarship and to continue to support our early career researchers to focus on improving outcomes for women with preeclampsia and to understand its causes. The clinical translation work of the Group is supported by a grant from the South Western Sydney Local Health District (SWSLHD) as the Women's Health Innovation and Translation Unit (WHITU).

OUR IMPACT

Our research goals are to better understand the causes of preeclampsia. By measuring the functions of the placenta and predicting preeclampsia, we seek to provide new, safe treatment that would allow the pregnancy to progress to full term, thus reducing the burden of premature delivery and also, long term, the risk to women's heart health. Our work is directly translatable to women in pregnancy, resulting in an immediate impact through translational research efforts. Our Group has a strong international and national reputation for the quality and effect of our research plans. If preeclampsia could be prevented, then one of the strongest risk factors for women's heart disease could also be prevented or reduced. This is an important long-term goal for women's heart health.

Professor Makris is the current president of the Australia & New Zealand Preeclampsia craft group, SOMANZ (Society of Obstetric Medicine of Australia & New Zealand), and Professor Hennessy is the President elect of the international equivalent, the ISSHP (The International Society for the Study of Hypertension in Pregnancy).

RESEARCH PROJECTS

The role of placenta antibodies in causing blood vessel damage and hypertension
A study of 351 women enrolled in a past preeclampsia study, this work also involves growing placentas in the laboratory and looking at the impact of specific antibodies on placental growth.

The potential for placental growth to prevent and reverse preeclampsia
Placental growth factor is a recently discovered protein originating in the placenta, which is responsible for blood supply and oxygen to the placenta and baby. Placental nutrition is also being studied by examining the role of beta-adrenergic receptors in the placental protein metabolism.

Safer prolongation of pregnancy
A study of placenta growth and treatments that provide for a safer prolongation of pregnancy without premature delivery.

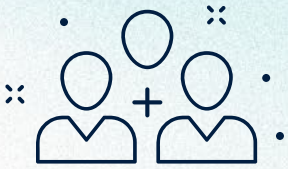
The pharmacology of aspirin in preeclampsia
Aspirin as a useful drug to prevent preeclampsia is being examined in terms of patient acceptability, drug dosing and its effect in preeclampsia prevention in a wide population across Sydney and south western Sydney.

Novel drug treatment for early severe preeclampsia
In partnership with major researchers in the USA, the Group is investigating the effect and safety of new biological treatments targeting the placenta for use in early severe preeclampsia.

Find out more: www.hri.org.au/our-research/vascular-immunology

Fundraising

Donations in 2020



72,062 generous donors from Australia, NZ and the UK supported HRI

7 gifts in Wills received

6 major gifts from donors and corporate donors

5 gifts from trusts and foundations

Report 2020

COVID-19 has been enormously challenging for the entire community, and while thankfully our scientists were able to continue their important investigations with minimal interruption, the challenges for the Institute as a whole have been truly unprecedented.

Nowhere was the disruption of COVID-19 more profound than amongst our fundraising programs. As many of the states shut their borders and some states entered hard lockdowns, HRI's public fundraising activities had to be suspended. This meant we were unable to meet donors face to face, host events, run public fundraising programs or conduct tours of the Institute.

As many of us adapted to working from home, home schooling kids and holding online meetings, our fundraising team quickly adapted to the additional challenges of fundraising remotely. And while our team's ability to continually stay one step ahead of the virus was noteworthy, the true heroes of this crisis were our wonderful donors.

In the face of tremendous uncertainty around their jobs, their finances and fears of contracting COVID-19 themselves, our donors maintained their selfless commitment to support HRI's critical research themes. It's hard to imagine greater generosity than to continue to give during such a tempestuous time. Thank you so very, very much. Thank you also to the Walter & Eileen Ralston Trust, who supported Dr Ashish Misra in his research into understanding how colchicine protects against atherosclerosis.

I'd also like to make particular mention of those very special donors who remembered the HRI with a gift in their Will. These are amongst our most special gifts, as we often get to engage with the surviving family members and hear about the life of their loved one and why supporting medical research was so important to them. From all of us, thank you for your eternal generosity.

Finally, if there is one positive from the past 12 months of the global pandemic, it is that we've seen in real time what can be achieved when medical researchers focus their minds upon a major public health threat, and most importantly, are provided with the resources to move fast.

While we now have an effective vaccine for COVID-19, there's still so much to do for those suffering from cardiovascular disease. Thank you for coming on this important journey with us. We hope in the coming years to unravel many of the mysteries of cardiovascular disease. Without your support, this simply wouldn't be possible.

Thank you.

Richard Wylie
Director of Fundraising and Brand

Operations Report 2020

Dr Stephen Hollings
CEO

Due to the measures put in place, HRI was very well-placed to continue with its research activity, and this was maintained throughout the year with minimal interruption.

It was a very busy year worldwide and not least for everyone at HRI, with the arrival of COVID-19 early in 2020 and the required large-scale workplace changes to keep everyone safe while maintaining the daily operations of the Institute.

The Work, Health and Safety committee led by Dr Phil Morgan as well as the Executive team played a significant role in navigating the many safety, health, operational and financial challenges. Due to the measures put in place, HRI was very well-placed to continue with its research activity, and this was maintained throughout the year with minimal interruption. The Operations and Fundraising teams operated under a hybrid arrangement of some working from home and some from the office, so that social distancing and NSW Health requirements could be met.

In early 2020, prior to the arrival of COVID-19 in Australia, HRI was very pleased to host our fifth Australian and New Zealand Summer Scholarships program. This program received excellent feedback and resulted in several students staying on for Honours and considering a PhD with HRI in future years.

In late 2020, HRI conducted its first Employee Engagement Survey, through consultancy firm Voice Project, to run a "temperature check" to understand where HRI was doing well as an organisation and where we could make improvements. Employees were asked to rank HRI's performance on multiple indicators such as recruitment, teamwork, supervision, workload, risk reporting, vision and values. Despite the impact of the pandemic, HRI was thrilled to receive a Best Workplace Award in November 2020 for providing an exceptional work environment for staff, which only 10 per cent of Voice Project's clients attain. The results were benchmarked against those of other Australian medical research institutes, and it was found that HRI outperformed the benchmark by an average of 11 per cent for those questions that had industry benchmarking. In addition, HRI secured an 80 per cent average score for all indicators.

Finance

INCOME

The revenue HRI received from Australia and overseas for 2020 was $20.1 million (FYR19: $24.6 million). Revenue from government grants and fundraising (including bequests) in 2020 declined by 33 per cent and 13.5 per cent respectively when compared to the previous year's results.

Other income of $1.97 million in 2020 was $1.68 million better when compared to FYR 2019. This was principally due to the Federal Government's JobKeeper and cash boost subsidies of $1.59 million. HRI was entitled to receive this additional financial support from the government due to the decline in its revenue resulting from the impacts and implications of COVID-19.

EXPENDITURE

Operating expenditure of $19.4 million during the year was 22.48 per cent lower when compared to the costs incurred in 2019. Fundraising costs of $3.84 million were 51.46 per cent, or $4.07 million lower than in 2019.

OPERATING RESULT

The Institute's results from operating activities plus net investment income less lease interest and foreign currency translation differences was a total comprehensive income of $3.03 million. This result was $1.15 million better when compared to the results in 2019.

FINANCIAL POSITION

The net asset position of HRI as at 31 December 2020 was $45.25 million. This consisted of $20.52 million in current assets, $15.72 million in investments, $14.85 million in net fixed assets, $1.61 million in right-of-use assets and $7.45 million in total liabilities.

Cash and short-term investments of $19.34 million, together with managed investments of $15.72 million, place the Institute in a very strong position to continue its campaign against cardiovascular disease in future years.

A copy of our full annual financial report is available from our website or by contacting HRI at support@hri.org.au.

Technology

The IT team has been pursuing a cloud-first strategy for a number of years, and this certainly paid off when COVID-19 reached Australia and much of HRI began working from home. Unlike many other organisations, few changes were required to our infrastructure to support remote workers in a secure manner. This enabled our researchers and operations staff to transition quickly and continue working with minimal changes to IT procedures and processes.

Virtual meetings and collaboration increased significantly at HRI in 2020. IT deployed Microsoft Teams for meetings and phone calls, replacing Skype for Business, and this platform has been used to facilitate team meetings and discussions, as well as virtualising large-scale meetings and events that were previously only physical. IT facilitated virtual HRI Town Hall meetings, scientific seminars, and two Student Open Days.

In 2020, IT also deployed LabArchives, an electronic lab notebook platform, increasing the ability for scientists to access their research data in multiple locations and to collaborate much more easily than with traditional physical notebooks. When a new research group joined HRI, LabArchives made it very simple to transfer research data from one institution to another.

In 2021, IT will continue to pursue a cloud-first strategy as much as possible, minimising the management of on-premise infrastructure and maximising flexibility. We look forward to leveraging technology to bring greater efficiencies to both the scientific and administrative areas of HRI.

Despite the impact of the pandemic, HRI was thrilled to receive a Best Workplace Award in November 2020.

Sustainability

In 2020, a significant saving of $60,000 was achieved in the utilities budget due to a strong focus on improving plant and equipment efficiency.

The sustainable building elements of HRI, such as the 375-panel solar system, the 50,000 litre rainwater tank for bathroom re-use, and an advanced building management system, all combined to help reduce our electricity, water and gas usage.

These savings also had a positive effect on the environment by reducing our carbon footprint by 240 tonnes of CO_2 emissions compared to previous years.

Notable Awards 2020

Landslide win for HRI

Eight of HRI's scientists were recognised as world leaders in their fields by being awarded NSW Health Cardiovascular Research Capacity Program grants. The coveted grant was awarded to Professors Shaun Jackson, Angela Makris and David Celermajer, Associate Professors Simone Schoenwaelder and Sanjay Patel, and Drs Freda Passam, Paul Coleman and Lining (Arnold) Ju.

Dr Katrina Giskes

Dr Giskes received the NSW & ACT Dr Charlotte Hespe Research Award for her outstanding work as a General Practitioner by GP Synergy. With her research group, Dr Giskes has come up with an innovative approach for patients to self-screen for atrial fibrillation (AF) at screening stations situated in GP waiting rooms that can integrate with the existing practice software and workflows. As many people with AF have no or very mild symptoms, these screening stations could help pick up abnormalities in patients' heartbeats that may otherwise go undetected.

Dr Lining (Arnold) Ju

Dr Ju was named a Eureka Prize finalist as an outstanding early career researcher in recognition of his excellent scientific research, leadership and engagement. Dr Ju was also awarded the Australian Institute of Policy and Science's Young Tall Poppy Science Award for his research excellence and public outreach. In addition, Dr Ju won the prestigious Sir Zelman Cowen Universities Fund Award for how he used his skills in biomechanical engineering to help solve crucial blood-clotting problems.

Dr Ashish Misra

Dr Misra was awarded a Perpetual IMPACT grant for his research understanding how the drug colchicine protects against atherosclerosis. Previously, Dr Misra made a groundbreaking discovery that changed our understanding of the way atherosclerosis progresses, revealing that certain smooth muscle cells (SMCs) migrate into atherosclerotic plaque and differentiate into cells called macrophages, which make plaque unstable. Dr Misra's work tests his hypothesis that colchicine promotes the regression of atherosclerosis because it causes the migratory cells to turn back into regular SMCs and therefore stabilises the plaque.

Dr Xuyu Liu

Dr Liu received the Sydney University Cardiovascular Initiative (CVI) Catalyst Award, a seed grant for EMCR-led multidisciplinary projects aligned to the clinical needs of cardiovascular patients across the Sydney Health Partners. The project is for research into the development of safer and more effective antithrombotics for the treatment of stroke. Dr Liu also received a grant from Therapeutic Innovation Australia: Pipeline Accelerator COVID-19 Rapid Response Funding for his research project "Towards the development of more effective and safer high-affinity ACE2 variants for the treatment of COVID-19".

Dr John O'Sullivan

Dr O'Sullivan was awarded the 2020 Future Leader Fellowship from the Heart Foundation, injecting much needed funds into his research into HFpEF, a common form of heart failure. HFpEF (Heart Failure with preserved Ejection Fraction) has become the commonest type of heart failure globally, and patients typically only survive around two years from diagnosis. Currently, there is no cure. The funding will aid further understanding of the condition and potential future therapy.

Dr Jessica Orchard

It was a blockbuster year for Dr Orchard, who in 2020 completed her PhD titled 'Atrial Fibrillation Screen, Management and guideline Recommended Therapy (AF-SMART II) in the rural primary care setting: a cross-sectional study and cost-effective analysis of eHealth tools to support all stages of screening'. For her talk on this study, Dr Orchard won the Cardiac Society of Australia & New Zealand Prevention Prize. She also won the Emerging Researchers in Mobile Health Prize at eHealth@Sydney 2020, and an educational grant for the European Heart Rhythm Association 2020 Congress. She was nominated for a Peter Bancroft Prize as her PhD was awarded without emendation, and was awarded best 8-minute PhD presentation by the Australian Society for Medical Research NSW.

Board of Governors

The Board of Governors is chaired by Professor Len Kritharides and comprises a representative of the Deans of the Medical Schools of Australia, nominees from the Sydney Local Health District and The University of Sydney, leaders from the corporate sector, and the Director of Cardiovascular Research of the Heart Research Institute.

The Board is responsible for the governance of the Heart Research Institute. It approves and monitors budgets and scientific progress. Members are balanced to represent the corporate and scientific community. The majority of the Board positions are available to be filled via election by the members of the incorporated company, the Heart Research Institute Ltd. Read the bios of our Board Members here.

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Heart Research Institute
2020 Annual Review

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