Auckland Medical Research Foundation

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ANNUAL REPORT 2021

SUPPORTING MEDICAL RESEARCH FOR OVER *65 years*

MIGRAINE TREATMENTS AND VISUALISATION

This image was inspired by migraine aura - colourful abstract patterns that can be part of the migraine experience. There is much to uncover about the cell biology behind migraine, like understanding the role of bubble-like structures called endosomes. Our research could help refine recently approved treatments for migraine.

Recently approved migraine treatments have put the spotlight on the neurohormone calcitonin gene-related peptide (CGRP). Deeper understanding of the full spectrum of CGRP signalling mechanisms, including receptor regulation will pave the way for further drug development. In their article, which received cover image status, Hay and colleagues reviewed CGRP and related peptide receptor regulation, highlighting the implications of this research for CGRP therapeutics. The cover image ties together two aspects of the review – the abstract colours and patterns of migraine aura with endosome-like bubbles.

Read more in the publication listed on page 29.

Image designed by Erica R. Hendrikse and Charlotte E. Johnson, School of Biological Sciences, University of Auckland for article: Gingell JJ, Hendrikse ER, Hay DL. New insights into the regulation of CGRP-family receptors. Trends in pharmacological sciences. 2019 Jan 1;40(1):71-83.

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PRESIDENT'S REPORT 2021

The year 2021 was another remarkable one – remarkable as the second year where coronavirus dominated our lives and remarkable with the stories of resilience and commitment as our scientists navigated nearly 200 days (since 2020) of lockdown disruptions in our Auckland region.

For our Auckland-based researchers, the February 2021 move to Alert Level 3 and the ten-week lockdown in mid-August meant they were unable to work in their laboratories and all patient studies were put on hold.

As always, the support from our donors meant AMRF was able to respond to our research community in their greatest time of need, and at the end of 2021 a $1.36million emergency Covid-19 Relief Fund was launched. This provided researchers working on 73 impacted projects with access to additional funding support to keep a roof over their heads and put food on the table while recommencing their vital research.

In 2021, our relentless pursuit of our mission continued with the awarding of the Douglas Goodfellow Repatriation Fellowship to Dr Emma Nolan, a major up-and-coming research talent in the field of breast cancer research. Dr Nolan (featured on page 4) worked in internationally recognised institutions in Australia and England for the last ten years. In her time offshore, Emma and her teams discovered a potential preventative medication to combat the aggressive breast cancer gene mutation BRCA1 and a new connection between cancer cells and a special type of immune cell. Dr Nolan's return to Auckland will see her establishing a laboratory collecting breast tumour samples, the first of its kind in New Zealand, which can be used by researchers across the country to advance breast cancer research.

In addition to Dr Nolan's fellowship, we awarded the AMRF Senior Research Fellowship for the second time since its inception, to the University of Auckland's Dr Amy Chan. Dr Chan's research combines artificial intelligence and big data to identify new ways of discovering if asthma is getting worse in patients and detecting life-threatening exacerbations before they occur. Two AMRF postdoctoral fellowships, the Ruth Spencer Medical Research Fellowship and four doctoral scholarships, were also awarded (featured on pages 6 to 9), including a second Helen Goodwin Doctoral Scholarship before the first scholarship has been completed. The Kelliher Charitable Trust (KCT) again provided two KCT Emerging Researching Start-Up Awards to AMRF postdoctoral fellowship recipients.

Every year I find it challenging to put into words the immense difference you, our donors, make, but the stories of hope, discovery and medical advancements you will read about in the ensuing pages are testimony to your generosity and commitment to improving the lives of others.

My sincere thanks extend to our Executive Director, Sue Brewster and the AMRF team who bring our mission to life on a daily basis.

To the Trustees, Commitee Chairs and Committee Members, I thank you for your gifts of time and expertise which makes it possible for our researchers to carry out their best work. I would particularly like to acknowledge the contribution of Christine Ding who stepped down from the AMRF Board after more than ten years of wonderful service and welcome Dr Anna King and Katie Noble to our Board.

My final thank you is to the Goodfellow family and their associated charitable trusts which fund all of AMRF's operational expenses. This support ensures every donor dollar goes directly into research which transforms our lives today, tomorrow and for generations to come.

Richard Taylor

President

MEDICAL COMMITTEE REPORT 2021

With the Covid-19 pandemic still gripping the world, it was incredibly pleasing to be able to support our world-class medical researchers with the awarding of nearly $4.25M in grant funding.

Our highly skilled AMRF Medical Committee voluntarily assessed 159 applications, of which 47 were awarded across a multitude of research themes. Particular highlights from this year was the ability to support so many personal awards, as outlined in the President's Report. The continuing strong relationship with the Kelliher Charitable Trust saw the awarding of two Kelliher Charitable Trust Emerging Researcher Start-up Awards, bringing the total awarded to 17 since 2014.

The launch of a Covid-19 Relief Fund was another highlight which was in response to our Auckland research community nearing crisis point. While we had been able to provide time-only extensions for them to try to complete their research, their salaries were also running out. Due to lockdown delays, many researchers were well behind where they should have been and the Relief Fund provided the opportunity to apply for the equivalent of three to six months' of the total salary component in their original grant.

Examples of research impacted by Auckland lockdowns was Professor Larry Chamley's two-year investigation into what triggers preeclampsia. This project was significantly delayed by hospitals having strict isolation rules in place, restricting the ability to get access to the laboratory and to receive an estimated 50 human placentas intended to be tested within hours of delivery.

The launch of the Covid-19 Relief Fund and awarding of 2021 grants would not have been possible without the dedication and expertise of our volunteer Medical Committee members and co-opted members. These highly skilled professionals ensure a contestable and robust assessment process is followed for all applications. It is a testament to their commitment to medical research they were able to achieve this whilst still managing their own research, clinical and teaching responsibilities throughout this pandemic.

In 2021, we welcomed Professor Ashvin Thambyah from Department of Chemicals & Materials Engineering, and Dr Raewyn Poulsen from Department of Pharmacology & Clinical Pharmacology, both at the University of Auckland. Their expertise will add great value to the already diverse experience of our Medical Committee. I also extend my gratitude to A/Prof Evelyn Sattlegger for her input into the Committee over many years.

On behalf of the Medical Committee, I would like to thank the AMRF team, under the expert guidance of Sue Brewster. In particular, my sincere thanks go to Dr Hannah Gibbons (Research Programme Manager) for her stewardship of the Grants Portfolio and management of the Medical Committee in a time when the committee has had to adapt to pandemic constraints.

I would also like to thank our Board of Trustees, under the outstanding Presidency of Richard Taylor, for their hard work and belief that funding the highest quality medical research will improve the health of New Zealanders, and our loyal supporters who are a vital part of our AMRF mission.

Professor Peter Browett
Chair, Medical Committee
Professor of Pathology, Department of Molecular Medicine and Pathology, The University of Auckland; and Haematologist, Auckland District Health Board

RETURNING HOME TO ESTABLISH A NEW BANK OF TUMOUR ORGANOIDS

Dr Emma Nolan

Auckland Cancer Society Research Centre, The University of Auckland

OBESITY AND BREAST CANCER: A NOVEL 3D ORGANOID MODEL TO STUDY CANCER-ADIPOCYTE CROSSTALK ($407,591 - 2 years) 1421001

Dr Emma Nolan was awarded the AMRF Douglas Goodfellow Repatriation Fellowship in 2021, allowing her to return home after ten years of working in the globally recognised Francis Crick Institute (London) and Walter & Eliza Hall (Melbourne). Coming home to New Zealand to set up a research lab had always been a career goal of Emma's, applying the expertise and knowledge she had gained through her international work in a local context.

There are two phases to Emma's work back in Auckland with the first priority to establish her own research team and a bank of tumour organoids – mini tumours in a dish – which will represent a cross section of breast cancer in New Zealand. The new 'bank' will be used by Emma for her own research but will be available for scientists across the country to advance breast cancer research.

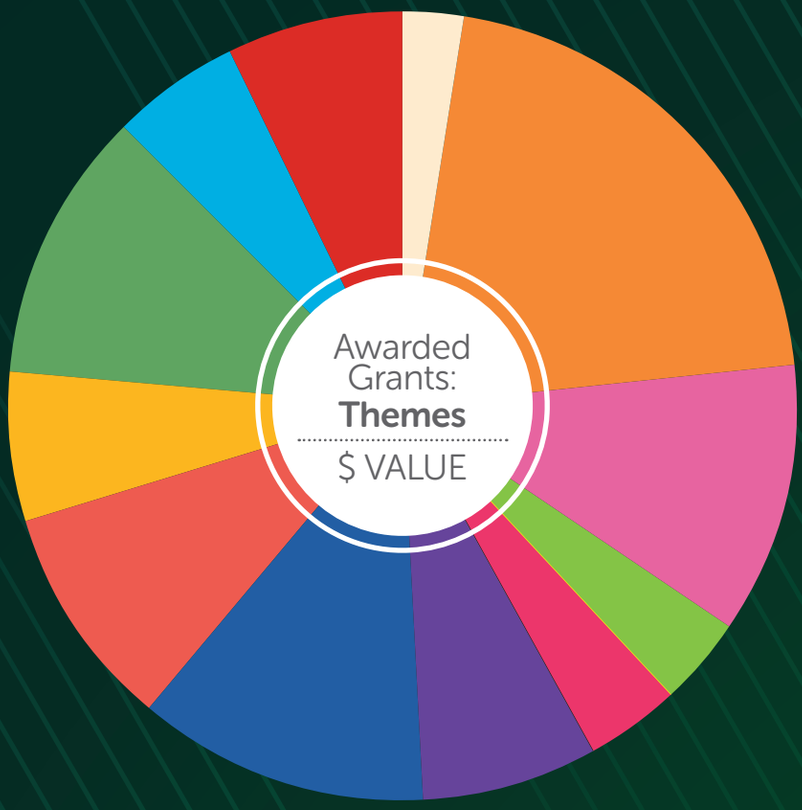
The second phase will be using the organoids in a relatively unstudied area of breast cancer research – the link between obesity and cancer progression.

"It's very well known that patients with obesity typically do much worse from cancer – they have larger tumour size, they have more advanced disease and they respond less well to therapy – but it's not understood how breast cancer cells interact with fat cells and how this drives the growth. I hope to identify new pathways in which we could perhaps treat patients and open up new avenues for therapy," explained Emma.

FUNDED BY: Douglas Goodfellow Charitable Trust

"If it hadn't been for the AMRF Douglas Goodfellow Repatriation Fellowship, I would probably still be in the UK, unable to share my knowlege and experience to benefit New Zealand directly."

GRANTS AWARDED



2021 AWARDED GRANTS — THEMES
47 GRANTS AWARDED TOTALLING $4,248,102

- Biomedical Imaging (1) | **$113,016** | 2.66%
- Cancer (8) | **$881,363** | 20.75%
- Cardiovascular Science (5) | **$474,952** | 11.18%
- Cellular & Molecular Biology (2) | **$157,948** | 3.72%
- Endocrinology, Metabolism and Nutrition (1) | **$865** | 0.02%
- Infection and Immunity (2) | **$161,743** | 3.81%
- Musculo-skeletal Science (1) | **$1,080** | 0.02%
- Neuroscience (5) | **$307,289** | 7.23%
- Other (8) | **$499,436** | 11.76%
- Population Health (3) | **$398,795** | 9.39%
- Pulmonary, Renal, Nephrology & Gastrointestinal Sciences (2) | **$259,505** | 6.11%
- Reproduction, Development, Maternal & Newborn Health (4) | **$465,711** | 10.96%
- Sensory Sciences (2) | **$ $226,661** | 5.34%
- Surgery (2) | **$299,810** | 7.06%

(n) Number of grants
$ Value each theme
% Total expenditure

POSTDOCTORAL FELLOWSHIPS

EDITH C. COAN RESEARCH FELLOWSHIP

EFFECTS OF HEARING ON BALANCE ($201,690 - 2 years)

1321001

Dr Rachael Taylor

Dept. of Physiology,
The University of Auckland

Maintaining balance equilibrium is key in reducing the risk of falls and improving the quality of life for people with inner ear balance disorders, particularly those who also have hearing loss.

The maintenance of balance is a complex physiological process that depends on the integration of information from many senses, particularly vision, proprioception (sensing muscle and joint movement), and input from motion sensing (vestibular) organs of the inner ear. Disorders of these vestibular organs are a common cause of imbalance, leading to reduced mobility, decreased independence, and an increased risk of falls.

Interestingly, there is growing evidence that our sense of hearing interacts with vestibular input from the inner ear and preliminary evidence indicates it could be used to supplement impaired vestibular function in the maintenance of balance and spatial navigation.

Dr Taylor aims to understand the complex interaction of hearing and vestibular function in spatial awareness and maintenance of balance. Understanding the interaction between hearing and balance could lead to novel and easily implemented hearing interventions to enhance balance rehabilitation and reduce falls risk.

FUNDED BY: Edith C. Coan Trust

perpetual guardian

AMRF POSTDOCTORAL FELLOWSHIP

CULTIVATING BETTER MENTAL WELLBEING FOR REFUGEES ($214,184 - 2 years)

1321002

Dr Zarintaj (Arezoo) Malihi

Dept. of Counselling, Human Services and Social Work,
The University of Auckland

Ensuring the provision of equitable health services to all is a public health priority and a human right. This becomes more accentuated with minority groups who have been forcibly displaced from their home country due to persecution, conflict, and war. The awarding of this fellowship will allow Dr Malihi to examine large data from different government agencies to identify and measure the mental wellbeing of refugees in New Zealand.

Arezoo aims to develop this understanding by applying statistical models to refugees' mental health status, service access rates, and wider settlement outcomes related to employment and education. This would help us to begin to understand what can be learnt from currently available data and what essential data is missing. This knowledge will inform future studies that would take refugees' voices into account; an essential component to improving refugees' mental health. Results of this research will inform policy and practices to improve better settlement outcomes for this minority group. The methodological novelty holds further promise that this measure of wellbeing could be used for other minority groups, including Māori and Pacific peoples.

MEDICAL RESEARCH FELLOWSHIPS

RUTH SPENCER MEDICAL RESEARCH FELLOWSHIP

LONG-TERM EFFECTS OF ANTENATAL CORTICOSTEROID EXPOSURE ($302,000 - 3 years) 1421003

Dr Anthony Walters

Liggins Institute, The University of Auckland

This project aims to understand the later life effects of antenatal corticosteroid treatment for threatened preterm birth. Corticosteroids are recommended for women at risk of preterm birth to reduce breathing problems and improve survival of their babies. However, it is not known if there are long-term health effects of this treatment. The first study in the world to assess the effectiveness of corticosteroids was done in Auckland between 1969-1974. Dr Walters will study the now 50 year old children of mothers who took part in that study, and also their own children, using questionnaires, routinely collected data and clinical assessments. The findings will determine whether corticosteroid treatment has effects on later health and wellbeing, including that of the next generation, to help improve future life-long care of those born preterm.

FUNDED BY: Ruth Spencer Estate

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DOUGLAS GOODFELLOW MEDICAL RESEARCH FELLOWSHIP

MECHANISMS OF POST-SURGICAL GASTRIC ARRHYTHMIAS ($104,000 - 1 year) 1421004

Dr Tim Hsu-Han Wang

Dept. of Surgery,
The University of Auckland

Many upper gastrointestinal (GI) procedures are performed for several indications, such as for obesity or cancer. In New Zealand, the Māori population has a higher obesity prevalence of 48.3%. The most common post-surgical symptoms experienced include nausea, vomiting and indigestion. Recent technological advancements have allowed researchers to identify the presence of electrical waves in the stomach, similar to that in the heart. These electrical activities are controlled by nerve cells in the stomach wall, known as the Interstitial Cells of Cajal (ICC). Abnormalities in these electrical waves have been attributed to GI symptoms. Electrical changes following gastric surgery have yet to be identified. Recently, a new technique called Body Surface Gastric Mapping (BSGM) has enabled researchers to take recordings by applying an electrode array onto the skin, similar to an ECG, without any need for surgery. This study will be the world's first, with Dr Wang using BSGM on patients undergoing upper GI surgery to determine the electrical changes that occur following surgery. The study will also assess ICC networks at the GI anastomosis in pig models. The results from this study will undoubtedly open a new window into GI function and have the potential to affect millions of patients worldwide undergoing GI surgery.

FUNDED BY: Douglas Goodfellow Charitable Trust

DOCTORAL SCHOLARSHIPS

IDENTIFYING THERAPEUTIC TARGETS AND BIOMARKERS ASSOCIATED WITH DISTINCT ALPHA-SYNUCLEIN POLYMORPHS ($131,000 - 3 years) 1221004

Mr Kreesan Reddy

Dept. of Anatomy & Medical Imaging,
The University of Auckland

Synucleinopathies are a collective of neurodegenerative diseases characterised by lesions of misfolded α-synuclein (α-Syn) aggregates. Parkinson's disease (PD) is the most well-known synucleinopathy affecting an estimated 10 million worldwide. It is presently the fastest-growing neurodegenerative disease, with the number of global patients increasing from 2.6 to 6.3 million between 1990 and 2016. Multiple System Atrophy (MSA) is a less common disease that presents remarkably similar to PD in the clinic. As such, approximately 20% of patients diagnosed with PD are found to have MSA upon autopsy, with the converse occurring in patients diagnosed with MSA. At present, there are no biomarkers or disease-modifying treatments for PD and MSA. Current treatments address symptoms of disease, eventually becoming ineffective in the late stages of disease. It is thought that the shortcomings of these treatments are based on their use after significant neurological damage has occurred. Mr Reddy's research hopes to identify potential biomarkers and therapeutic targets that enable the distinction and treatment of specific synucleinopathies early in the disease. It is estimated that delaying the onset of neurodegenerative disorders by one year can reduce the number of cases by 11%; therefore, providing new therapeutic targets and biomarkers may help reduce disease burden in the future.

PANCREATIC EXOCRINE INSUFFICIENCY: ADVANCING DIAGNOSIS AND TREATMENT ($131,000 – 3 years) 1221001

Mrs Kylie Russell

Dept. of Surgery, The University of Auckland

Pancreatic exocrine insufficiency (PEI) occurs when the quantity of digestive enzymes released into the small bowel is insufficient to ensure normal absorption of food. Untreated PEI results in micronutrient deficiency, malnutrition, poor quality of life and reduced survival. PEI develops in 56–98% of patients following surgical resection of the pancreas (pancreaticoduodenectomy (PD)). PD is the only potentially curative treatment for head-of-pancreas cancer, other cancers (ampullary, bile duct and small bowel cancers), chronic pancreatitis and other non-cancerous pancreatic tumours. The foundation of treatment for PEI is pancreatic enzyme replacement therapy (PERT); however, patients are undertreated and guidelines regarding when and what dose to commence PERT are conflicting. Mrs Russell will use an international survey, regarding current prescribing of PERT in patients following PD, to develop an education module for practitioners to address gaps in knowledge. A randomised controlled trial will establish a) whether pre-emptive, routine, treatment with PERT post PD improves nutritional status and quality of life, and b) which dose (low vs high) provides maximal benefit. The project will determine the prevalence of micronutrient deficiency post PD, which is currently unknown, and develop guidelines for clinicians regarding screening and treatment protocols. The project will also test the safety of administering PERT in patients with a compromised gut through a rodent model of PD.

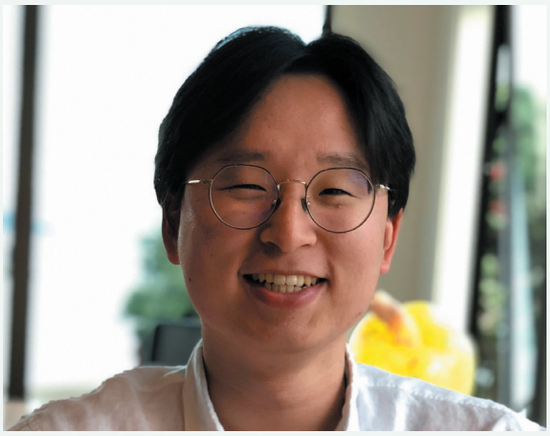
DOCTORAL SCHOLARSHIPS continued

A NOVEL BRAIN IMPLANT FOR PATIENTS WITH HYDROCEPHALUS ($131,000 – 3 years) 1221005

Dr Sang Ho-Kim

Auckland Bioengineering Institute,
The University of Auckland

Imagine being a parent and told that your child has an abnormal build-up of fluid around the brain (hydrocephalus), which will require neurosurgery to install a tube (shunt) to drain the excess fluid. Initially, you are relieved that there is treatment, but you are told that there is a 60% chance the shunt will block within the first two years. The consequence of shunt blockage is a life-threatening increase in pressure inside the head. Frequent visits to the Emergency Department ensue as the signs of shunt failure are subtle and can look like the common cold. Shunt failure can only be confirmed with a brain scan. Thus, having a shunt means living in a perpetual state of anxiety, not knowing when it will fail, and being exposed to radiation every time it is suspected. A team of engineers, neurosurgeons, and Dr Ho-Kim want to remove that stress, unnecessary radiation exposure, and the likelihood of missing shunt malfunction by developing a tiny brain implant that senses and wirelessly transmits pressure measurements inside a person's head. This project aims to prove the implant is safe and suitable for the intended purpose, culminating in a first-in-human safety study.



HEALTHEX EMERGING RESEARCHER AWARDS

AMRF Outstanding Emerging Researcher Award $3,000 6721004

Dr Robyn May

Auckland Bioengineering Institute,
The University of Auckland

A computational model to identify cardiovascular remodelling related to prematurity and predict later cardiovascular risk.

AMRF Doctoral Oral Presentation Runner up Award $2,000 6721005

Mr Wenxuan Chen

Dept. of Molecular Medicine & Pathology, The University of Auckland

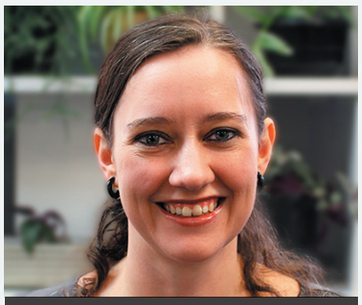
IGF signalling mediates lymphatic vessel growth in zebrafish.

AMRF Best Poster Presentation Award $2,000 6721006

Miss Phoebe Burns

Auckland Cancer Society Research Centre, The University of Auckland

Investigating the influence of hypoxia on cGAS-STING signalling in macrophages.



Dr Robyn May

Mr Wenxuan Chen

Miss Phoebe Burns

Grants Awarded

ELIMINATING GROUP A STREPTOCOCCUS ($160,000 – 2 years) 1121008

Dr Alan Cameron, Dr Jia-Yun Tsai, Prof Thomas Proft, Dist Prof Dame Margaret Brimble

School of Chemical Sciences,
The University of Auckland

Dr Alan Cameron

Group A Streptococcus (GAS) is a human pathogen responsible for a number of diseases, including acute rheumatic fever (ARF) and rheumatic heart disease (RHD). These diseases are the cause of significant mortality and morbidity globally, with Māori and Pacific children in New Zealand amongst the most heavily impacted. GAS can become internalised inside host epithelial cells, forming intracellular reservoirs that allow it to evade the host immune system and drug treatment. This internalisation is associated with treatment failure and recurring GAS infection. The current antibiotics (e.g. amoxicillin) used to treat GAS infection, fail to penetrate host epithelial cells and new cell permeable treatments are desperately needed. Some antimicrobial peptides (AMPs) have recently been identified to penetrate human cells without significant toxic effects, but their usefulness is often limited by poor half-life. Peptide stapling is a modern approach to improve the biological stability of AMPs and importantly, is established to enhance mammalian cell penetration. However, the ability of stapled AMPs to eradicate internalised bacteria (e.g. GAS) is yet to be investigated. Using a novel and improved peptide stapling technique recently developed by the lead investigator, stapled AMPs will be prepared and investigated as new treatment strategies for intracellular GAS infections.

EXPERIENCES OF THE END OF LIFE CHOICE 2019 ACT AMONGST HEALTH PRACTITIONERS, WHĀNAU AND FAMILIES ($156,142 – 2 years)

1121014

Dr Gary Cheung, Dr Rosemary Frey, A/Prof Frederick Sundram, A/Prof Sarah Cullum, A/Prof Susan Bull, A/Prof David Menkes, Dr Nicholas Hoeh, Dr Alisha Vara, Dr Adam Sims, Dr Jackie Robinson, Dr Deborah Balmer, Dr Melissa Carey, Dr Helen Cassidy

Dept. of Psychological Medicine,
The University of Auckland

Dr Gary Cheung (l) and Dr Rosemary Frey

The End of Life Choice 2019 Act (the Act) came into force in New Zealand on November 7, 2021. The Act provides a framework for people experiencing unbearable suffering from a terminal illness to have the option of requesting medical assistance to end their lives. The Act is likely to create many legal, ethical, clinical, and social ripples as it is implemented. This project has two aims. The first is to explore the experiences of health practitioners involved in assisted dying and allow reflection on their experiences. International studies have shown that participation in assisted dying has significant emotional and psychological effects on the involved practitioners. The second aim is to gain a more complete picture of the Act's impacts by exploring perspectives of whānau/family of assisted dying. This project has potential to uncover knowledge and service gaps in provision of the Act, along with understanding emotional and other impacts of assisted dying on health practitioners and whānau/families. A knowledge translation plan will be developed to expand knowledge and capacities amongst key stakeholders and recommend changes in practice informed by the project findings.

NATURE'S PACEMAKER ($159,859 - 2 years)

1121003

Dr David Crossman, Dr Jizhong Bai, Dr Kyriakos Varnava, Dr Angus Grey, Dr Rohit Ramachandra, Prof Julian Paton

Dept. of of Physiology,
The University of Auckland

Dr David Crossman

Human heart failure is the inability of the heart to pump enough blood to meet the energetic demands of an active lifestyle. This condition results from cardiac muscle cells losing their ability to generate force. This is a serious health condition and a major cause of death in New Zealanders. In this research, we will investigate a novel pacemakers ability to reverse remodel the pathological changes that damage the electrical connections responsible for signalling muscle cell shortening that generates force. In particular, we are interested in characterising the changes in collagen remodelling that is responsible for damaging these electrical connections, a finding we identified in previous research supported by the Auckland Medical Research Foundation. Moreover, we will identify which molecules interact with collagen VI, how they change in heart failure and reverse with treatment with our pacemaker. This will be achieved with state-of-the-art super-resolution microscopy and mass-spectrometry to provide both a visual and molecular analysis.

CONNEXIN 43 AND PRETERM BRAIN INJURY ($159,351 – 2 years) 1121016

Dr Justin Dean, Dr Joanne Davidson, Prof Alistair Gunn, Dr Panzao Yang

Dept. of Physiology,
The University of Auckland

Dr Justin Dean

This study examines why premature babies have a high risk of neurodevelopmental impairment in later life. We have shown experimentally that exposure to infection/inflammation can impair growth of the brain, consistent with clinical findings. We will test the central hypothesis that inflammation-induced opening of small channels in the brain (called hemichannels) is a key regulating event that triggers impairment of brain development. We will dissect the role of hemichannels using a newborn model of low dose injection of inflammatory molecules and treatment with connexin hemichannel blocking peptides. This new knowledge will underpin the development of new treatment strategies for infection-related brain damage.

FEMALES IN AOTEAROA WITH ISCHEMIC HEART DISEASE AND ACUTE CORONARY SYNDROMES (FAIR-ACS) ($125,835 – 2 years) 1121009

Dr Nikki Earle, Prof Rob Doughty, Dr Katrina Poppe, Dr Anna Rolleston, A/Prof Malcolm Legget

School of Medicine
The University of Auckland

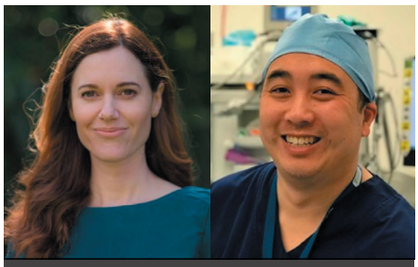
Dr Nikki Earle (l) and Prof Rob Doughty

Improved treatments mean more people are surviving events such as heart attacks, and are then living with heart disease. Recurrent events for these people are common, with nearly 30% dying or being readmitted to hospital for related causes within one year of their first heart attack. Despite being a leading cause of death for women, historically there has been significant under-representation of women in heart disease research studies and the evidence base for therapies is less in women than it is for men. In this study of 800 women admitted to New Zealand hospitals with a first-time heart attack, we will measure a number of heart biomarkers (including genetic markers of heart disease risk), as well as the known clinical and environmental cardiovascular risk factors such as nutrition, stress, and physical activity. This will help us to better understand how heart attacks manifest differently in women compared with men, and to identify risk markers for subsequent events that are specific to women, leading to more personalised and better targeted treatments and more equitable health outcomes for women with heart disease in New Zealand.

PHARMACOKINETICS OF PERIOPERATIVE LIGNOCAINE ($64,810 - 2 years) 1121015

Dr Jacqueline Hannam, Dr Daniel Chiang, A/Prof Malcolm Tingle

Dept of Pharmacology & Clinical Pharmacology, The University of Auckland



Dr Jacqueline Hannam (l) and Dr Daniel Chiang

Lignocaine infusions during and after surgery are increasingly popular to control pain, particularly in surgery for endometriosis, colorectal cancer and breast cancer. However, dosing is poorly defined and does not consider patient and surgical factors that may influence pharmacokinetics and clinical outcome. Current understanding of lignocaine pharmacokinetics (the relationship between dose and concentration) is inaccurate and outdated. Commonly used dosing regimens have resulted in plasma concentrations which may exceed the accepted toxic plasma concentration of 5µg/ml. The objective of this project is to develop robust pharmacokinetic model for lignocaine and its metabolite that will allow us to rationally adjust dose for different pain settings, populations, and over longer treatment durations without compromising patient safety. The study aims to characterise the pharmacokinetic profile of lignocaine and its primary active metabolite using population pharmacokinetic models. This is a prospective, observational, multicentre clinical study of 50 patients undergoing elective surgery within the Auckland region. Patients who are planned to receive intravenous lignocaine as part of their anaesthetic will be recruited. Patient and treatment factors and blood samples will be collected to develop a population pharmacokinetic model of lignocaine and its metabolite.

Grants Awarded continued

SYNTHETIC LETHALITY AND DNA DAMAGE RESPONSE ($159,636 - 2 years) 1121007

A/Prof Michael Hay, Dr Barbara Lipert, Dr Tet-Woo Lee, Dr Stephen Jamieson

Auckland Cancer Society Research Centre, The University of Auckland

A/Prof Michael Hay

Cancer cells use DNA repair mechanisms to escape the full effects of cytotoxic chemotherapy and radiotherapy. Our recent discovery of a new drug, SN39536, that inhibits a key repair enzyme, DNA-dependent protein kinase (DNA-PK), provides a new tool to potentiate cancer treatment with both modalities. This DNA-PK inhibitor could also be used in patients whose tumours have defects in the DNA repair genes, a very common feature of cancer cells that results in metastasis and therapy resistance. We are seeking to identify which particular tumour mutations will combine with the drug to kill the tumour cells. We will use a gene-editing approach to individually inactivate every gene involved in DNA repair and then monitor the effect of SN39536 alone, or in combination with chemotherapy or another DNA repair inhibitor. The identification of effective drug-mutation combinations will provide a path to clinical use of SN39536 in cancer patients whose tumours harbour these defined mutations. This approach is likely to have reduced side effects compared to conventional chemotherapy or radiotherapy.

FUNDED BY: W & WAR Fraser Bequest Fund

FROM CRISIS TO RECOVERY: PROTECTING CHILD HEALTH AND WELL-BEING THROUGHOUT THE PANDEMIC ($159,611 – 2 years) 1121012

A/Prof Annette Henderson, Prof Nickola Overall
Dept. of Psychology
The University of Auckland

(Top l-r) Prof Nickola Overall, A/Prof Annette Henderson, Dr Rachel Low; (Bottom l-r): Nina Waddell, Caitlin McRae, Dr Valerie Chang

As NZ moves through the COVID-19 crisis to recovery, the long-term impact of the pandemic is of pressing concern. The pandemic has involved stressful challenges that continue to pose a threat to health and well-being. The scientific community has documented the health costs of the pandemic but has overlooked the family processes that may undermine or protect children's health and well-being during this challenging time. The current research answers an urgent call to identify ways to address the costs of pandemic-related family disruptions to children's health and well-being. Leveraging an existing family study, we will track the health and well-being of NZ families prior to the pandemic, during the Level 4 lockdown, and two years into the pandemic to identify the family risk processes (inter-parental conflict, poor parenting) that increase the risk of detrimental health and well-being outcomes for children. We will also identify the family resilience processes (family cohesion, co-operative co-parenting) that buffer the health and wellbeing costs of the pandemic. The results will offer valuable insight into how to cultivate family resilience in the face of stress and insecurity, thereby improving the health and quality of life of NZ families and their children.

BM12 CAST STUDY: CYCLOPHOSPHAMIDE AFTER SIBLING-DONOR ALLOGENIC STEM-CELL TRANSPLANTATION ($98,982 - 2 years) 2121012

Dr Clinton Lewis, Dr Richard Doocey, Dr Timothy Hawkins, Prof Peter Browett, Dr Nicole Chien
Cancer and Blood Services,
Auckland District Health Board

Dr Clinton Lewis

Acute leukaemia and myelodysplasia are the cause of most bone marrow transplants worldwide. This study aims to prove that a drug called cyclophosphamide works better than current standard of care at reducing the side effects and preventing graft-versus-host-disease (GVHD) in bone marrow transplant patients. Currently, 40% of bone marrow transplant patients develop GVHD and 5-10% die within a year of transplant. While their initial disease is cured, many surviving patients suffer with the terrible effects of this painful, debilitating disease. The BM12 CAST study is a randomised clinical trial conducted in the hospital setting. It is the only study of its kind testing this new treatment to reduce side-effects and improve the quality of life for post-transplant patients and positive results will have an important impact on international treatment practice.

FUNDED BY: Anonymous

THE INFLAMMASOME AND DIABETIC RETINOPATHY ($155,995 – 2 years) 1121013

Dr Odunayo Mugisho, Dr Rinki Murphy

Dept. of Ophthalmology,
The University of Auckland

Dr Lola Mugisho

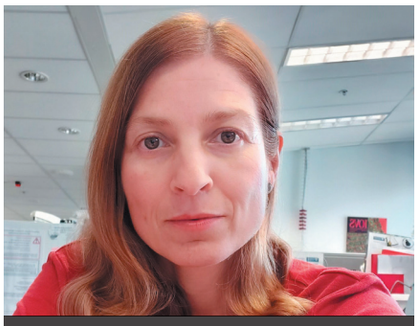
Diabetes is one of the most common health problems in New Zealand affecting over 250,000 New Zealanders. It is associated with several complications one of which is diabetic retinopathy (DR), a chronic disease that can lead to vision loss. While there are a range of therapies currently available, these only treat late-stage DR signs without slowing the disease progression. Previous work done in our lab and by others have identified a new disease mechanism, the inflammasome pathway, that plays a role in the development and progression of DR. Furthermore, we have shown using several disease models that blocking this pathway using our anti-inflammasome drugs can prevent the development of DR. In the proposed study, we hope to use human donor eye tissues and blood samples to better understand how the inflammasome contributes to DR progression and to determine the best time to treat patients to prevent or reverse disease signs.

FUNDED BY: Marion Ross Memorial Fund

VERIFICATION AND FUNCTIONAL CHARACTERISATION OF AQP3 IN THE LENS ($113,016 – 2 years) 1121011

Dr Rosica Petrova, Prof Paul Donaldson, Dr Julie Lim

Dept. of Physiology,
The University of Auckland



Dr Rosica Petrova

Despite safe and effective surgical treatments, lens cataract is still the leading cause of blindness in the world today. This is in part because researchers do not completely understand how the lens maintains its transparent and refractive properties over many decades of life. Research by our laboratory has shown that in the absence of a blood supply the lens generates a circulating flux of water that maintains lens functionality. They have proposed these water fluxes are a target for the development of novel medical therapies to treat cataract. The water flows in the lens are mediated by several different water channels from the Aquaporin (AQP) family of proteins, which are critical to the maintenance of lens transparency. Recently, we have identified an additional water channel, AQP3, in the lens. Unlike the other lens AQPs, AQP3 has unique properties that implicate it in the removal of hydrogen peroxide, a known oxidative stress that has been linked to the initiation of cataract. Hence, by studying AQP3, we will determine not only the role of AQP3 in the lens, but whether it is a potential target for the development of novel anti-cataract therapies.

COVID-19 VACCINATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE - NEW ZEALAND (C-VAK NZ study) ($159,505 - 12 months) 2121006

A/Prof Helen Pilmore, Dr Michael Collins, Dr Ian Dittmer, Prof Germaine Wong, Dr Paul Manley, Dr Sally Roberts

Dept. of Renal Medicine,
Auckland District Health Board

A/Prof Helen Pilmore

Aotearoa New Zealand is in a unique position internationally due to our low community exposure to the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). Hence we can expect that very few dialysis or kidney transplant recipients will have immunity to COVID-19. Vaccination is expected to be undertaken in 2021. Dialysis and kidney transplant recipients are often less able to mount an immune response to vaccination. In addition, vaccination can stimulate anti HLA antibodies and cause acute antibody mediated rejection in transplant recipients and reduce the likelihood of acceptable transplant matches for patients on dialysis waiting for a transplant. We plan to measure the serological response to the COVID-19 vaccination in patients on dialysis and after kidney transplant in order to determine if these patient groups have a lower response to vaccination. Additionally we will identify whether patients awaiting kidney transplantation develop new anti HLA antibodies after vaccination.

Grants Awarded continued

PACE C: INTERNATIONAL RANDOMISED STUDY OF CONVENTIONALLY FRACTIONATED RADIOTHERAPY VS SBRT FOR ORGAN-CONFINED PROSTATE CANCER ($68,320 - 1 year, 5 months) 2121005

Dr Giuseppe Sasso, Dr Maria-Lee Pearse

Radiation Oncology Department,
Auckland District Health Board

Dr Giuseppe Sasso

Prostate cancer is the most common cancer affecting men in New Zealand. Traditionally prostate cancer was treated with radiation over a period of seven to eight weeks. The impact of prolonged treatment in terms of increased hospital visits and its effect on the budget is quite significant. Recent evidences have shown that it can be effectively treated over four weeks safely and has thus been adopted as the standard of care. PACE C aims to reduce it further to just five fractions. This would allow the patients to return to normal life faster and bring down the economic and psychological burden. Moreover, the positive effect on the radiotherapy services nationwide is substantial. The reduction in the treatment duration results in an increased capacity for the radiation units thereby allowing us to treat more patients in any given time and as such faster access to healthcare by all. Ultimately, this provides easy access for all to the best services, in a timely manner to improve overall cancer outcomes. Despite a large body of evidence for SBRT (Stereotactic Body Radiotherapy) in prostate, PACE C is the first randomised trial comparing these two radiation schedules and its results can change the present standard of care.

ANTIBIOTIC HYBRIDS AGAINST AMR ($159,991 – 2 years) 1121018

Dr Andrew Thompson, Prof Greg Cook, Dr Veronica Playle

Auckland Cancer Society Research Centre, The University of Auckland

Dr Andrew Thomspon

Antimicrobial resistance (AMR) arises when bacteria, fungi, parasites or viruses change over time and develop the ability to ward off the drugs designed to destroy them, making the treatment of infections difficult or even impossible. AMR is recognised as one of the leading threats to global health, currently resulting in about 2000 deaths daily, with fatalities predicted to skyrocket more than 10-fold within the next 30 years. In New Zealand, infections caused by multidrug-resistant microorganisms are increasing, with the overuse of antibiotics and travel from regions with higher AMR levels (like South-East Asia) exacerbating the problem. Our research will utilise a different approach to drug design, where two complementary antibiotics are linked together into a single molecule. This approach offers several potential advantages, including better potency and safety, and a reduced chance of generating resistance; there are now several candidates of this type in clinical trials. By linking two drugs from a newly approved regimen to treat multidrug-resistant tuberculosis, we have already been able to demonstrate superior antibacterial activity, including against resistant strains. Our study will optimise the design and physical properties of these "antibiotic hybrids", aiming to develop a more effective and safer drug to treat severe bacterial infections.

ARRHYTHMOGENIC CALCIUM LEAK IN DIABETES ($158,143 – 2 years) 1121010

Dr Marie-Louise Ward, Dr Kenneth Tran, Dr Amelia Power, Prof Peter Ruygrok

Dept. of Physiology,
The University of Auckland

(l to r) Anna Krstic, Dr Amelia Power, Paige Karanikolaou, Dr Marie-Louise Ward (seated)

Type 2 diabetes (T2D) is one of the largest and fastest growing health issues within New Zealand and is closely linked with the development and progression of cardiovascular diseases, including cardiac dysfunction, arrhythmias and heart failure. Our study focuses on the calcium cycling changes that occur in the heart's contractile cells, cardiomyocytes. Each heart beat is triggered by coordinated calcium release within cardiomyocytes. Clearance of calcium within cardiomyocytes between beats (diastole) is equally important for proper relaxation to enable refilling of the heart. When calcium release occurs between beats this is known as 'diastolic calcium leak'. Our recent research has revealed that atrial tissue from diabetic patients have increased diastolic calcium leak and contract more weakly than tissue from non-diabetic patients. These observations warrant further investigation since diastolic calcium leak in animal models of heart disease has been shown to drive progression to heart failure, trigger fatal cardiac arrhythmias, promote muscle damage and decrease exercise capacity. The overall aim of this project is to identify and target cellular and molecular triggers that promote diastolic calcium leak in human atrial tissue from diabetic and non-diabetic patients. This information will be invaluable in identifying strategies to protect the hearts of diabetics.

rEPO AND HYPOTHERMIA FOR NEONATAL ENCEPHALOPATHY ($160,000 - 2 years) 1121001

Dr Guido Wassink, Prof Alistair Gunn, Prof Laura Bennet

Dept. of Physiology,
The University of Auckland

Dr Guido Wassink

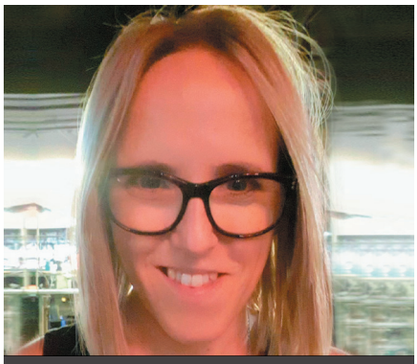
In New Zealand and around the world, perinatal oxygen deprivation remains a major cause of neonatal death and lifelong disabilities such as cerebral palsy. These outcomes are devastating for individuals, families and caretakers, and place significant burden on finite healthcare and educational resources. Therapeutic hypothermia (mild brain cooling) was developed in New Zealand and is now standard treatment for perinatal brain damage from oxygen deprivation, to improve infant survival without disability. However, hypothermic protection is partial: nearly half of infants either still die or develop disabilities, despite brain cooling. Thus, new strategies that can further improve neurological outcomes are critical. Recent evidence suggests that recombinant erythropoietin, a pleiotropic growth factor, can support survival of injured brain cells, and help promote repair of the newborn brain after oxygen deprivation. It is not known if recombinant erythropoietin can improve outcomes after hypothermia. This project will use the same clinically-relevant model of oxygen deprivation in the developing brain that helped establish therapeutic hypothermia, and tests whether giving recombinant erythropoietin after therapeutic hypothermia is better than cerebral cooling alone. This will provide critical information that will guide future clinical trials.

FUNDED BY: Curtis-Tonkin Paediatric Fund

VAPOR-C TRIAL ($142,668 - 2 years) 2121004

Dr Anna Waylen, Prof Tim Short, Dr Doug Campbell, Dr Greg O'Grady, Dr Ben Lawrence, Dr Sarah Nicolson

Anaesthesia Department,
Auckland District Health Board



Dr Anna Waylen

Each year 25,000 people in New Zealand are diagnosed with cancer, with a large number undergoing surgical treatment under anaesthesia. Alarmingly, early evidence suggests that the type of anaesthetic drugs used during surgery can affect cancer spread, patient survival and the risk of experiencing long-term pain after surgery. Recent studies show that traditional inhaled (volatile) anaesthesia may have a negative effect on the body's defence systems, resulting in worse outcomes after cancer surgery. Early evidence suggests that the more recent alternative anaesthetic drugs propofol (total intravenous anaesthesia) and local anaesthetic lignocaine infusion may protect the immune system, thereby reducing cancer metastasis, improving patient survival and decreasing chronic pain after surgery. We are participating in an international trial to identify if widely used anaesthesia drugs can improve outcomes in patients undergoing surgery for bowel or lung cancer. Bowel cancer and lung cancer are the two highest causes of cancer death in New Zealand, with almost 3000 New Zealanders dying from these diseases each year. We believe that this study has the potential to drastically improve patient well-being and population health for a large number of New Zealanders.

FUNDED BY: Anonymous

USING IN-SITU SIMULATION TO RESOLVE THREATS TO PATIENT SAFETY ($46,000 – 2 years) 1121017

Prof Jennifer Weller, Dr Carlos Campos, Dr Jennifer Long, Ms Kaylene Henderson, Dr Andrew MacCormick, Prof Alan Merry

Centre for Medical and Health Sciences Education, The University of Auckland

Prof Jennifer Weller

In 2016, ACC funded implementation of an innovative, national simulation-based team training programme for all public hospitals: NetworkZ. The simulations are run in the actual workplace, simulating real clinical challenges, and testing both teams and systems. NetworkZ has transformed the capacity for simulation-based training for hospital staff across all public hospitals providing a valuable avenue for preparing to deal with future challenges in healthcare. Alongside this team training, we have identified multiple potential threats to patient safety, like missing, faulty, or inadequate equipment; lack of common understanding of protocols such as response to massive bleeding or trauma team activation; and gaps in staff knowledge and training. Though many faults have been resolved, there remains ongoing challenges in systematically learning from threats and ensuring they are fixed and no longer a potential cause of harm to patients. In this study, we aim to proactively identify underlying threats in the operating and emergency departments. We also aim to develop a national threat reporting system through an in-depth exploration of factors that facilitate or impede resolving these threats. It will improve identification of threats (by standardised in-situ simulations) and resolve these potential threats to patients through a national approach to quality improvement.

Grants Awarded continued

KELLIHER CHARITABLE TRUST AWARDS

EMERGING RESEARCHER START-UP AWARD $14,769 1721002

Dr Marie-Claire Smith

Dept. of Medicine,
The University of Auckland

Dr Marie-Claire Smith

This award will provide research support for Dr Marie-Claire Smith's Postdoctoral Fellowship entitled 'TWIST 3: Validation of the Time to Walking Independently after STroke tool'.

FUNDED BY: Kelliher Charitable Trust

Kelliher Charitable Trust

EMERGING RESEARCHER START-UP AWARD $30,000 1721003

Dr Nikki Earle

Dept. of Medicine,
The University of Auckland

Dr Nikki Earle

Research support for Dr Nikki Earle Postdoctoral Fellowship titled 'Multi-omics and biomarkers to personalise risk prediction and therapy in acute coronary syndromes''.

FUNDED BY: Kelliher Charitable Trust

Kelliher Charitable Trust

SUMMIT POSTDOCTORAL RESEARCH SYMPOSIUM

BEST POSTDOCTORAL RESEARCH PRESENTATION AWARD $3,000 6721003

Dr James McKeage

Auckland Bioengineering Institute,
The University of Auckland

Dr James McKeage

AMRF Best Research Presentation Award: Needle-free capillary blood sampling using jet injection.

AMRF SUPPORT OF WAITEMATĀ DHB RESEARCH WEEK

$500 Award 6721001
Dr Karen Bartholemew

Planning Funding and Outcomes, Waitematā District Health Board; Auckland District Health Board

Excellence in Research Award - Best Senior Researcher at the 2021 Waitematā DHB Health Excellence Awards: Māori perspectives on a potential lung cancer screening programme.

$500 Award 6721002
Dr Joanna Hikaka

School of Pharmacy,
The University of Auckland

Excellence in Research Award - Best Emerging Researcher at the 2021 Waitematā DHB Health Excellence Awards: Development of a pharmacist-facilitated medicines review intervention for community-dwelling Māori older adults in Aotearoa New Zealand.

SIR HARCOURT CAUGHEY AWARD

$24,971 1721001

Dr Chen (Peter) Qui

Dept. of Physiology,
The University of Auckland

New insights into presbyopia – Developing and validating a spin test device to measure regional differences in lens stiffness.

$25,000 1721004

Dr Julie Spray

Dept. of Physiology,
The University of Auckland

How Do Children and Families Negotiate Roles in Asthma Self-Management?

TRAVEL GRANTS

Due to the impact of Covid-19 on worldwide travel, many conferences have been postponed, cancelled or shifted to an online format. Where possible, researchers have been encouraged to reschedule their travel†, attend an on-line meeting#, or decline* their award if no alternative exists.

Dr Emma Buckels ($1,953 – 6621007)†

Dept. of Molecular Medicine & Pathology,
The University of Auckland

To attend MEDSCI NZ and the Advances in Microscopy satellite meeting, Queenstown, New Zealand, 29 August - 4 September 2021.

Mrs Robin Cronin ($711 – 6621001)

Middlemore Hospital,
Counties Manukau District Health Board

To attend the 32nd International Confederation of Midwives Virtual Triennial Congress. 30 May – 3 June 2021.

Dr Zohreh Doborjeh ($897 – 6621008)†

Section of Audiology,
The University of Auckland

To attend AWCBR, Queenstown, New Zealand, 29 August - 5 September 2021.

Dr Jui-Lin Fan ($1,115 – 6621003)†

Dept. of Physiology,
The University of Auckland

To attend MEDSCI NZ, Queenstown, New Zealand, 29 August - 3 September 2021.

Dr Rosemary Frey ($803 – 6621010)

School of Nursing,
The University of Auckland

To participate in the virtual Oceanic Palliative Care Conference 2021, online, 7 - 9 September 2021.

Dr Christopher Hedges ($865 – 6621006)†

Dept. of Nutrition & Dietetics,
The University of Auckland

To attend Queenstown Molecular Biology conference, and associated Metabolic and Heart Research satellite meeting, Queenstown, New Zealand, 29 August - 6 September 2021.

Dr Augusto Simoes-Barbosa ($1,743 – 6621009)

School of Biological Sciences,
The University of Auckland

To attend the 16th Congress of the Federation of Asian and Oceanian Biochemists and Molecular Biologists, Christchurch, New Zealand, 22 - 25 November 2021.

Dr Sheryl Tan ($1,272 – 6621002)†

Dept. of Anatomy & Medical Imaging,
The University of Auckland

To attend AWCBR, Queenstown, New Zealand, 29 August - 5 September 2021.

Dr Ted Yeung ($1,008 – 6621004)

Auckland Bioengineering Institute,
The University of Auckland

To attend MEDSCI NZ, Queenstown, New Zealand, 31 August - 5 September 2021.

Dr Yuliana Yosaatmadja ($1,666 – 6621005)

School of Biological Sciences,
The University of Auckland

To attend the 16th Congress of the Federation of Asian and Oceanian Biochemists and Molecular Biologists, Christchurch, New Zealand, 22 - 25 November 2021.

SIMULATING SURGERIES TO SAVE LIVES

Prof Jennifer Weller

AMRF Project Award Recipient

Professor Jennifer Weller and her team are helping resolve over 200 latent safety threats for patients, identified following real-to-life simulations in 21 operating theatres across New Zealand.

AMRF awarded Prof Weller $123,000 for a pilot study in 2012 that springboarded her to a five year, multi-million dollar Accident Compensation Commission contract. The contract was for the delivery of training to every district health board in New Zealand, using a life-like human simulator and potential traumas, with a train-the-trainer programme.

The simulations have identified latent safety threats – low frequency but high pressure events that threaten patient safety – such as missing, faulty, or inadequate equipment, a lack of understanding of protocols such as response to massive bleeding or trauma team activation and gaps in staff knowledge and training.

It is a life-saving tool. There have been many examples of similar actual cases following the simulations, with the team using what they learnt.

"Though many of these faults have been resolved, there remains an ongoing challenge in learning from these threats and ensuring they are fixed and are no longer a potential cause of harm to patients," Jennifer says.

Read more on page 15.

GRANTS COMPLETED

RURAL CHILDREN: REGIONAL VS URBAN RISK OF APPENDICITIS COMPLICATIONS – DR BRODIE ELLIOT

Completed Doctoral Scholarship
($18,000 - 1 year) 1218003

Dept. of Surgery, The University of Auckland & Northland District Health Board

Appendicitis is the most common reason children require emergency surgery. Delayed presentation to hospital increases chances the appendix perforates, leading to increased pain, hospitalisation and complications. This burden of perforation is unequally distributed in overseas studies but remains uninvestigated in New Zealand. We first interviewed rural Northland families who had presented to hospital for their child's appendicitis. Delay in getting to hospital was commonly a result of a protracted decision-making phase where families considered their resources and balanced care for other children. Families with reduced financial or social resources were more likely to 'watch and wait' due to the increased relative cost of accessing hospital. We then undertook a clinical study in 14 hospitals across New Zealand. Clinical data was supplemented by a parental questionnaire. The total rate of perforated appendicitis was 38.5% and was significantly higher in Māori (54.8%) and rural children (44.1%) The children with perforated appendicitis had a much higher duration of prehospital symptoms (47.8h vs. 20.1h). Our project has demonstrated inequity in the outcomes of paediatric appendicitis in New Zealand. Increased severity of paediatric appendicitis is independently associated with rural patient status and Māori ethnicity. Despite a superficial focus on equity, accessing healthcare is frequently financially damaging and unpleasant for Māori.

FUNDED BY: Curtis-Tonkin Paediatric Fund

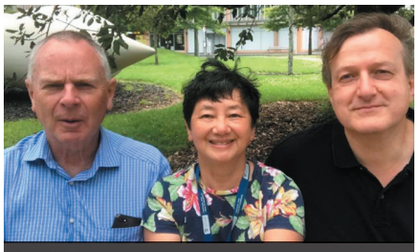
Grants Completed

PROJECTS

HBeAg SEROCONVERSION ($123,428 – 2 years) 2115001

Dr William Abbott

New Zealand Liver Transport Unit, Auckland District Health Board



(l - r) Dr William Abbott, Dr Euphemia Leung and Dr Klaus Lehnert

The purpose of this project was to determine whether proteins from the C open reading frame of the hepatitis B virus (HBV) suppress the immune response to the virus, allowing cirrhosis and liver cancer to develop. We have evidence from transfected HEK293 cells to show an inhibitory effect of the HBV pre-core protein (p22) on the innate immune response to the virus. We are now focused on identifying the molecular mechanisms responsible for this suppression; hoping that this will lead to new treatments for chronic hepatitis B. Our pull-down experiments found that p22 interacts with four proteins that regulate interferon production (C1QBP, PRDX4, TUFM and VCP). We are using siRNA knockout to assess the functional significance of these interactions. The possibility that a C1QBP-p22 interaction results in lower interferon production is excluded. There has been a change in behaviour in two of our control cell lines which prevent the other siRNA molecules being studied. We are investigating the cause of this change, initially with ATAC methylation studies, to find out the cause of the problem.

FUNDED BY: John and Poppy Stilson Endowment Trust

NOVEL PEPTIDE ANTIBIOTICS TARGETING ANTIMICROBIAL RESISTANCE ($159,824 – 2 years) 1118013

Dr Ghader Bashiri, Dr Paul Harris, Dr Stephen Ritchie

School of Biological Sciences, The University of Auckland

Dr Ghader Bashiri

During the course of this project, we combined our expertise in enzyme technology and synthesis of complex peptide natural products to produce lexapeptide analogues. This was based on the rationale that we will use chemical synthesis to produce a partially modified precursor peptide, which will then be fully 'matured' using enzymatic tools to perform the steps that are challenging to achieve synthetically. We have characterised four enzymes that collectively install the two complex ring systems in lexapeptide, Lan and AviMeCys. Our results provide a molecular understanding of these biosynthetic enzymes, which will subsequently be used in our pipeline for the preparation of lexapeptide and its analogues. In addition, our methodologies might also be used to produce other members of lanthipeptides that contain these exquisite structural motifs.

FUNDING CONTRIBUTION BY: Room-Simmons Charitable Trust and the Paul Stevenson Memorial Trust

perpetual guardian

MEASURING IN VIVO ACTIVITY IN THE AUDITORY CORTEX AND ITS LINK TO AUTISM SPECTRUM DISORDERS ($159,250 - 2 years)

1116009

Dr Juliette Cheyne, Prof Peter Thorne, A/Prof Johanna Montgomery

Dept. of Physiology & Centre for Brain Research, The University of Auckland

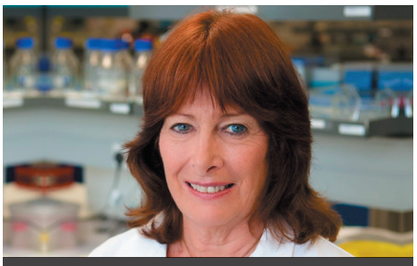
Dr Juliette Cheyne

Autism Spectrum Disorders (ASD) are defined by impaired learning, sensory disorders, communication difficulties, social deficits, and stereotyped behaviours. In ASD distorted processing of sounds is thought to underlie impaired language abilities. We hypothesise that auditory cortex circuitry develops incorrectly, resulting in abnormal neuronal connectivity and impaired ability to process sound. We are utilising in vivo calcium imaging to examine activity in the auditory cortex during early development and in adulthood in a mouse model of ASD. During the past year we have established a new technique for driving robust expression of genetically encoded calcium sensors in the whole mouse brain, enabling imaging of activity in from one week to several months of age. Additionally, we are developing a 'mesoscope' that will enable imaging of the entire mouse brain. We will utilise this new system to examine spontaneous activity in the developing brain in ASD. We previously found that cortical representation of sound is poorly organised in this model of ASD and our current experiments will reveal whether this difference stems from altered activity during early development. Together this will help us to understand how changes in the auditory cortex link to language impairments in ASD.

LACTOFERRIN IN PROSTHETIC JOINT INFECTIONS ($160,000 - 2 years) 1119002

Prof Jillian Cornish, Dr Simon Young, Dr Scott Bolam, Mr Stuart Irwin

Dept. of Medicine,
The University of Auckland



Prof Jillian Cornish

Joint replacement infections are a major challenge clinically due to the formation of bacterial biofilms on implant surfaces. Biofilms make bacteria resistant to antibiotics. This AMRF grant has enabled us to establish the rat joint replacement infection model and used both in vivo and ex vivo analysis to determine the bacterial burden and biofilm assessment. We demonstrated that using a milk protein, lactoferrin (LF), to treat infections that: LF breaks down biofilms, LF at low concentrations reduces bacterial load of strains of S.aureus (the most common bacteria found in orthopaedic infections), LF acts synergistically with antibiotics to double the antibiotic bacteriostatic effectiveness (prevents growth) and LF reduces the minimum bactericidal (killing) concentration of antibiotic by 10-fold.

INOSINE FOR BONE HEALTH ($160,000 – 2 years) 1118012

Prof Nicola Dalbeth, Dist. Prof Ian Reid

Dept. of Medicine,
The University of Auckland

Prof Nicola Dalbeth

The "Effects of Inosine Supplements on Markers of Bone Health" project is now complete. This was a clinical trial of 120 post-menopausal women in which participants received one of two treatments: inosine supplements or placebo. We studied a number of measures including markers of bone health and bone density of the skeleton. The key findings of the study were that although inosine supplements increased the blood urate levels, they did not affect the health of the skeleton. No changes were observed in cardiometabolic or kidney measures between the groups, and there were no differences in side effects between the two groups. While this study did not demonstrate a positive impact of inosine supplements on bone health, it has provided us very important information about urate biology.

CENTRAL CHEMOREFLEX IN HYPERTENSION ($159,215 - 1 year, 9 months) 1119008

A/Prof James Fisher, Prof Julian Paton

Dept. of Physiology,
The University of Auckland

A/Prof James Fisher

Our study aimed to better understand the mechanisms regulating blood pressure in people with high blood pressure (hypertension) to help the future development of new treatment strategies for this condition. Specifically, we investigated whether sensors within the body that detect blood oxygen and carbon dioxide become hyperactive, and drive up blood pressure by increasing the activity of the sympathetic nerves that constrict the arteries. Our kind AMRF funding provided salary support for a postdoctoral researcher that helped us establish an experimental facility to simultaneously monitor blood pressure, breathing, blood flow and sympathetic nerve activity, which is the first of its kind in New Zealand. Our findings suggest that, contrary to some studies using animal models, an increase in the sensitivity of the sensors for blood carbon dioxide do not cause bigger sympathetic nerve and blood pressure responses in people with hypertension. However, we did observe distinct differences in the way that breathing, blood pressure and sympathetic nerve activity were controlled in men and women. Our translational studies are ongoing and remain important to understanding why people have high blood pressure and how this may differ in men and women.

Grants Completed continued

DOES CYREN DETERMINE RADIATION-INDUCED TUMOUR MUTATIONAL BURDEN? ($156,091 – 2 years) 1118016

Dr Barbara Lipert, Prof William Wilson, Dr Francis Hunter, Prof Cristin Print

Auckland Cancer Society Research Centre, The University of Auckland

Dr Barbara Lipert

We previously identified the CYREN gene as contributing to resistance to DNA damaging radiation. In the present study, we generated CYREN knockout cells using CRISPR technology to investigate the mechanism(s) responsible, and whether CYREN expression influences cancer therapy outcome. We found that CYREN depletion impaired efficiency of DNA repair and resulted in an accumulation of genomic aberrations following irradiation, likely contributing to radiosensitivity. In contrast, CYREN depletion protected cells from cisplatin toxicity and was found to be a negative prognostic factor of serous ovarian cancer, where platinum compounds are frequently used. Based on analysis of CYREN loci in the CRISPR-manipulated cells, we deduced a possible mechanism regulating CYREN expression that involves a long non-coding RNA (lncRNA). Furthermore, we found that hypoxia, which is a prevalent feature of human tumours and negative impacts therapy outcome, downregulated CYREN expression probably via epigenetic modification of chromatin. Together, our findings suggest CYREN as a factor coupling hypoxia with therapeutic resistance and indicate regulation of CYREN expression as another layer of complexity in the DNA damage response in human cells.

FUNDED BY: Anonymous

CGRP AND BONE HEALING ($160,000 - 2 years) 1118008

Dr Brya Matthews, Dr Dorit Naot, Dr Christopher Walker

Dept. of Molecular Medicine & Pathology, The University of Auckland

Dr Brya Matthews (2nd from left) and her team

The goal of the project was to understand the role of a neurotransmitter known as CGRP in bone healing. This research is important as six inhibitors of CGRP have been approved by the US FDA for preventing or treating migraines since 2018, and it is likely that some of the patients receiving these therapies will experience bone fractures. The previous evidence suggested that sensory nerve signals including CGRP might be important for bone healing. We have found that male mice with no CGRP have bones that appear normal and have no changes in microarchitecture at the age we perform injury studies. However preliminary data suggests that healing in their bones might be impaired. Studies to confirm this are ongoing. We have shown that CGRP has positive effects on bone cells that respond to fracture, and we are in the process of examining what happens to sensory nerves and blood vessels during the rapid bone formation that occurs after injury.

STEREOTACTIC BODY RADIOTHERAPY IN LUNG METASTASES SAFRON II ($25,000 – 2 years) 2116004

Dr Giuseppe Sasso, Dr Shankar Siva, Mrs Rebecca Montgomery

Radiation Oncology, Auckland District Health Board

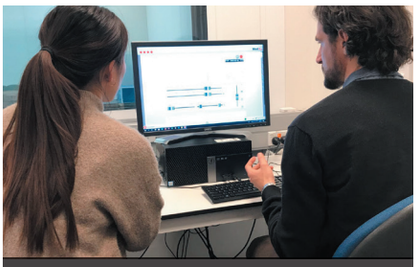
Dr Giuseppe Sasso

SABR is a new type of radiation therapy for treatment of certain small cancer tumours and can precisely target the cancer tumour to give a higher dose of radiation, while ensuring surrounding normal tissue receives minimal radiation. Treatment planning is more resource-intensive but can be delivered over fewer sessions for primary lung cancer. Compared to surgery, SABR can provide similar rates of tumour control and there is no need for hospitalisation. The primary endpoint of the study is grade 3 or higher AE related to treatment within one year of treatment. There were 38 patients in arm 1 (single-fraction) and 38 patients in arm 2 (multifraction) who were randomised. The number of grade 3+ AE related to treatment within 1 year in arm 1 and 2 were 2 (5% [80% CI: 1-13]) and 1 (3% [80% CI: 0-10]), respectively. Both arms met the safety criteria as the upper limit of the 80% confidence interval is below 17%. The number of grade 3+ AE was 8 (21% [80% CI: 13-32]) and 5 (13% [80% CI: 7-23]) in arm 1 and 2, respectively. None of the arms showed evidence of superior safety, efficacy or symptom burden compared to the other arm.

NEUTIN ARI ($104,556 – 2 years) 1118018

A/Prof Grant Searchfield, Prof Nikola Kasabov

Section of Audiology,
The University of Auckland



A/Prof Searchfield's audiology lab

The present study examined brain networks underlying tinnitus and its temporary elimination using sound. The research is helping us predict possible individual responses to treatment. Brain regions underpinning tinnitus change with sound exposure have been identified and mathematically modelled. Its clinical applications will in the future enable optimal and individualized treatment plans that are tailored specifically to the individual client based on artificial intelligence. A software app is being developed to implement the outcomes of this study as a tool for clinics to predict and select optimum treatments based on behavioral and brain measures. This is an exciting development as it will be a first of kind data driven tool for tinnitus research and therapy, that has the potential to revolutionize how tinnitus is treated, improving outcomes and reducing the use of treatments not suited to the individual.

FUNDING CONTRIBUTION BY:
Reed Charitable Trust

with you for generations to come Public Trust

BENZENESULPHONAMIDES: A PROMISING NEW CLASS OF IMMUNOSUPPRESSANTS ($158,808 – 2 years) 1118004

Dr Julie Spicer, Prof Geoff Hill, Dr Stephen Jamieson, Dr Kate Gartlan

Auckland Cancer Society Research Centre, The University of Auckland

Dr Julie Spicer and her team

The aim of this project was to identify and characterise potent and selective inhibitors of the protein perforin, a key component of the immune system. An effective blocker of perforin activity would represent an innovative immunosuppressive therapy that could potentially address rejection of bone marrow stem cell transplants. A large number of candidate molecules were designed, synthesised and tested for activity, with these results informing further rounds of optimisation. Advanced formulation studies were also carried out, resulting in a solid form of drug that was stable and able to be re-constituted as a solution suitable for intravenous formulation, a key requirement for critically ill patients requiring a bone marrow transplant. A subset of compounds was then further assessed for 'drug-like' properties (such as solubility) and three were selected for pharmacokinetic characterisation to inform studies in a preclinical mouse model of bone marrow stem cell rejection. Identification of two molecules optimised for pre-clinical testing was achieved. One compound was tested and showed moderate activity, while a second more promising candidate with increased potency and solubility will be subjected to preclinical efficacy testing in future studies.

INFLAMMATION AND COCHLEAR IMPLANTATION ($158,942 - 2 years) 1118002

Prof Peter Thorne, Dr Ravindra Telang, Dr Andrew Wise, A/Prof Srdjan Vlajkovic, A/Prof Phil Bird

Dept. of Physiology,
The University of Auckland

Prof Peter Thorne

A cochlear implant is a treatment of choice for those with a severe-to-total deafness that arises from the loss of sensory cells in the hearing organ of the inner ear. It is surgically inserted into the cochlea to stimulate remaining hearing nerves directly when sensory cells are missing through disease. However, post-surgery inflammation can lead to poorer implant performance especially in some patients. This research shows we can use MRI as a diagnostic tool in an animal model to assess inflammation following implantation and to assess the influence of anti-inflammatory drugs to reduce the inflammation and its consequences on implant performance. This may lead to biomarkers to determine the presence of inflammation for targeted treatment in humans.

FUNDED BY: W & WAR Fraser Bequest Fund

Grants Completed continued

SPACE CLUSTER RCT IN GENERAL PRACTICE ($150,012 - 2 years) 1117005

Dr Katharine Wallis, Prof Ngaire Kerse, Dr Linda Bryant, A/Prof C. Raina Elley

Dept. of General Practice & Primary Health Care, The University of Auckland

Dr Katharine Wallis

The aim of this project was to test the effect of the Safer Prescribing And Care for the Elderly (SPACE) on high-risk prescribing of non-steroidal anti-inflammatory drugs (NSAIDs) and/or antiplatelet medicines and related hospitalisations. We established a pragmatic cluster randomised controlled trial in general practice. Participants were patients at increased risk of adverse drug events (ADEs) from NSAIDs and/or antiplatelet medicines at baseline. SPACE comprised of automated searches to generate a list of patients for each general practitioner (GP) with high-risk prescribing; pharmacist outreach to provide education and one-on-one review of list with GP; and automated letter inviting patients to seek medication review with their GP. We recruited 21,877 participants, 1479 with high-risk prescribing. High-risk prescribing improved in both groups at six and 12 months compared with baseline. At six months, there was no significant difference between groups although SPACE improved more for gastrointestinal ADEs. At 12 months, the control group improved more. There was no significant difference for related hospitalisations. Further work is needed to identify scalable interventions that support safer prescribing in general practice. The use of automated search and feedback plus letter to patient warrants further exploration.

ACCESS TO ENDOSCOPY FOR MĀORI AT CMDHB ($10,580 - 6 months) 3120006

Ms Maree Weston, Dr Andrew MacCormick, Ms Emma Espiner, A/Prof Elana Curtis

Department of General Surgery, Middlemore Hospital, Counties Maunkau District Health Board

Ms Maree Weston

Counties Manukau DHB (CMDHB) has the highest rate of diagnosis of colorectal cancer at emergency presentation in NZ at 34%, which equates to a more advanced stage of disease, and worse overall survival. Māori present with colorectal cancer at a more advanced stage than other ethnic groups. A review of emergency presentations at CMDHB during 2016 showed that 11% of patients who were diagnosed at emergency presentation had been removed from the colonoscopy waiting list resulting in missed opportunities for an early diagnosis. This proposed study aimed to address whether inequities between Māori and non-Māori exist in access to endoscopy services at CMDHB. We published a literature review titled "Barriers and facilitators for Māori in accessing hospital services in Aotearoa New Zealand". We also performed quantitative analysis of referral and removal off the waiting list data at CMDHB endoscopy services over a one year period and this is being written up for publication in early 2022. Unfortunately, due to COVID-19 lockdowns we were unable to complete the qualitative analysis which involved structured interviews in the homes or maraes of people who did and did not successfully access endoscopy services. We have an obligation under tikanga not to put participants and whānau through unnecessary risk and it was deemed too risky to meet face-to-face.

FUNDED BY: Sir Lewis Ross Fund

NEUROCARDIAC ARRHYTHMIA MECHANISMS IN LQTS ($156,663 - 1 year, 9 months) 1119006

Dr Annika Winbo, A/Prof Johanna Montgomery, Prof Jonathan Skinner

Dept. of Physiology, The University of Auckland

Dr Annika Winbo

The project aims were to develop a human cellular model co-culturing sympathetic neurons and heart cells, using induced pluripotent stem cells (iPS cells) from healthy volunteers and long QT syndrome (LQTS) patients. Specifically, we wanted to characterise human sympathetic neurons in health and disease, and establish co-cultures of sympathetic neurons and heart cells, to learn more about the interaction between these cells in regulating heart rhythm and triggering arrhythmia. During the project, our team has successfully generated and characterised sympathetic neurons from healthy control iPS cells and LQTS patient iPS cells. Importantly, a novel hyperactivity phenotype was present in the LQTS sympathetic neurons. This neuronal hyperactivity may be an important contributor to sympathetically triggered arrhythmia in LQTS. Furthermore, we have successfully established human co-cultures of sympathetic neurons and heart cells. We showed that activating the neurons regulated heart rhythm in the co-cultures and could trigger arrhythmia signs in LQTS heart cells. This novel all-human co-culture model represents an important tool to study the interaction between sympathetic neurons and heart cells, in health and disease.

FUNDED BY: Bruce Cole Fund

COVID-19 RESEARCH AWARDS

EXOSOME-LIPOSOME HYBRIDS FOR TUMOUR TARGETED DRUG DELIVERY ($160,000 – 2 years) 1118019

A/Prof Zimei Wu, Dr Euphemia Leung, Prof Larry Chamley

School of Pharmacy,
The University of Auckland

A/Prof Wu (left) and research team

Nano-sized liposomes are perceived as 'magic bullets' for cancerous tumour-targeting and have been successful in clinical translation. However, challenges remain including their poor tumour tissue penetration, off target effects on healthy cells and slow release of drugs once in cells. In this project, we engineered a liposome (synthetic lipid nano scaled bubbles) – exosome (cell derived nano bubbles) hybrids to combine the beneficial features of both for targeted intracellular drug delivery to cancer cells, while sparing healthy cells. Our hybrids incorporated pH-sensitivity and a ligand to improve the ability for cytoplasmic release of drugs and tumour cell targeting. Despite the COVID-19 interruption which caused some loss of experiments, we established optimised methods for bioengineering the hybrids and understood the key factors affecting the hybridisation efficiency, and cellular/cytosolic release. The research has led to one review paper published and two manuscripts in preparation, and seven conference presentations. We would like to acknowledge that the AMRF funding has allowed the training of a 0.5FTE postdoc through the research and enabled a PhD student to complete the majority of their PhD project.

FUNDED BY: Anonymous

SARS-COV-2 VIRUS ENTRY INHIBITORS ($96,457 - 12 months) 1720007

Dist. Prof Dame Margaret Brimble, Dr Alan Cameron, Prof Miguel Quinones-Mateu, Mr Dan Fellner, Dr Allan Zhang, Dr Daniel Furkert, A/Prof Paul Harris

School of Chemical Sciences,
The University of Auckland

Distinguished Professor
Dame Margaret Brimble

SARS-CoV-2, the pathogen causing the worldwide COVID-19 pandemic, invades human cells through the binding of viral spike glycoprotein to human Angiotensin Converting Enzyme 2 (hACE2) receptor. Disrupting this protein-protein interaction (PPI) presents an important modality for therapeutic intervention. Therefore, we designed a series of stapled peptides as potential blockers of this PPI, mimicing the N-terminal helix of hACE2 protein containing most of the interacting residues at the binding site. Our in-house CLipPA technology enabled efficient instalment of peptide staple to enhance peptide shape. Initial biological assessment of a subset of our stapled peptides using a SARS-CoV-2 surrogate virus neutralisation assay showed negligible inhibitory activity against the binding between hACE2 and the virus spike protein. However, biological testing of the remaining compounds including the most helical double-stapled peptides is currently in progress and further evaluation of the anti-infective efficacy of the peptides in a cell assay against SARS-CoV-2 is also planned.

COVID-19 AND INTERRAI RESEARCH ($27,100 - 12 months) 1720014

Dr Gary Cheung, Dr Etuini Ma'u, Dr Claudia Rodriguez, Mr Adrian Martinez Ruiz, Professor Vanessa Burholt, Dr Brigid Ryan

Psychological Medicine,
The University of Auckland

Dr Gary Cheung

interRAI Home Care is routinely used in New Zealand to assess community dwelling for older adults who require support services because of their health issues and/or functional impairment. The main objective of this study is to compare the health outcomes of the interRAI population in the first year of the COVID-19 pandemic with the same outcomes in the year before COVID-19. We found the 80+ age group, females, Europeans and people who lived alone had better outcomes in the first post-lockdown quarter in terms of their self-reported mood, self-reported health and carer stress. However, the following groups had worse outcomes in the first post-lockdown quarter: (i) people who lived with others had worse self-reported health; and (ii) the 40-64 age group and people who lived with others had a significant increase in carer stress. We found no significant change in self-reported mood, self-reported health and carer stress in the second, third and fourth post-lockdown quarter. It appears that the first post-lockdown quarter was an adjusting period for the interRAI population and their carers, and there was no lasting negative effect on these health outcomes amongst the community dwelling interRAI population within the first year of the COVID-19 pandemic.

Grants Completed continued

(continued)

NURSE WELLBEING DURING COVID-19 ($31,494 - 12 months) 4720010

Dr Matthew Roskruge, Dr Margaret Brunton, Dr Catherine Cook

Massey Business School,
Massey University

Dr Matthew Roskruge

This project contributes to our understanding of the impact of COVID-19 on the wellbeing of the New Zealand nursing workforce, and the strategies that are adopted by nurses to ensure sustainability of the workforce and mitigate the stressors experienced during the pandemic. To achieve this, we adopt a mixed-methods approach including an online survey of a sample of New Zealand Nurses Organisation members, followed by qualitative online interviews occurring between October and December 2020. The key finding from this report is the identification of five primary themes relating to the intensity of the unique COVID-19 environment for nurses. These include: 1. Sense-making: nurses' retrospective process of trying to make sense of what was happening; 2. Relational dynamics: to enable them to navigate through the situation; 3. Care ethics: to allow them to provide ethical caring; 4. Human rights and health and safety breaches: in the midst of clear breaches of Human Rights; 5. Sustainability: these breaches threaten the sustainability of the public health service in New Zealand

JEAN CATHIE FUND FOR TINNITUS RESEARCH

SOMATSENSORY STIMULATION TO TREAT TINNITUS ($199,987 – 2 years) 7415002

Dr Yiwen Zheng

Pharmacology and Toxicology,
University of Otago

Dr Yiwen Zheng (right) and her research team

Tinnitus is a ringing, buzzing or roaring sound in a person's ear or a person's head without the corresponding external sound. Tinnitus can cause sleep disturbances, cognitive problems, work impairment and sometimes, even suicide. There is no effective treatment currently available. A previous study has suggested that the perception of tinnitus can be reduced by the stimulation of the somatosensory system and by precisely pairing the somatosensory with auditory stimulations. However, the effectiveness of this paired stimulation only lasts for a very short period. This project tested whether a modified paired stimulation protocol would achieve long-lasting suppression of tinnitus in a rat model of tinnitus and compared it with the paired stimulation protocol used in the previous study. To our surprise, none of the stimulation protocols were able to reduce behavioural evidence of tinnitus in rats. Further studies are needed to understand the discrepancy between our study and the previous study in order to develop effective treatment for tinnitus.

FUNDED BY: Jean Cathie Fund for Tinnitus Research

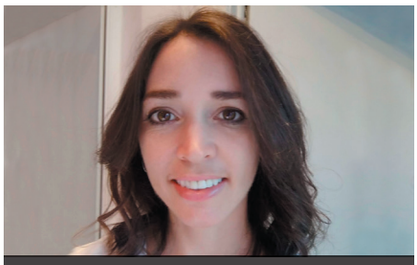
perpetual guardian

DAVID AND CASSIE ANDERSON RESEARCH FELLOWSHIP

ULTRASOUND IN ASYMPTOMATIC HYPERURICEMIA ($201,363 – 2 years) 1318001

Dr Sarah Stewart

Dept. of Surgery,
The University of Auckland



Dr Sarah Stewart

This fellowship aimed to explore the role of ultrasound in the transition from asymptomatic hyperuricemia (high urate levels) to symptomatic gout. A semi-quantitative ultrasound scoring system has been developed in collaboration with international rheumatology and ultrasound experts, and initial testing has shown this system to be reliable. This two-year fellowship has also provided the key foundation for a large five-year prospective multi-centre study which aims to determine the role of urate crystal deposition evident on ultrasound in the development of gout in people with high urate levels. A total of 15 national and international recruitment sites have been established across the globe, and despite Covid-19-related disruptions, 116 participants have been recruited into the study so far. The fellowship has also allowed the advancement of closely aligned projects related to the patient experience of gout flares, the diagnostic value of various imaging modalities for gout, and the predictive ability of urate testing for gout. This fellowship has resulted in a total of 10 publications in high-impact peer-reviewed journals and six international conference presentations.

FUNDED BY: David and Cassie Anderson Medical Trust

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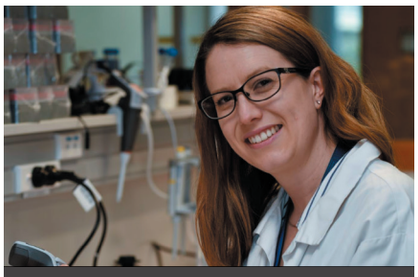
DOCTORAL SCHOLARSHIPS

BARBARA BASHAM DOCTORAL SCHOLARSHIP

MODULATION OF CALCITONIN RECEPTORS BY RAMPS ($126,500 - 3 years) 1215001

Dr Erica Hendrikse (nee Burns)

School of Biological Sciences,
The University of Auckland



Dr Erica Hendrikse

Amylin is a natural hormone that helps stabilize blood sugar levels and can reduce meal sizes. Mimicking amylin's effects is beneficial for people with diabetes and obesity. However, further development of amylin-based treatments requires a better understanding of how amylin works. Amylin activates regions of the brain, but the specific molecular targets needed for activation are unclear. In this study, I mapped amylin's molecular targets using antibodies as probes. I first confirmed the specificity of the antibodies using cell-based experiments. The antibodies were then used to probe rat brain tissue, generating fluorescent patterns that revealed the locations of amylin targets. The results from this project will inform further work into amylin-based diabetes and obesity treatments.

FUNDED BY: Barbara Basham Medical Charitable Trust

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AMRF DOCTORAL SCHOLARSHIP

KERATOCONUS IN DOWN SYNDROME ($97,890 – 2 years, 4 months) 1218001

Dr Joyce Mathan

Dept. of Ophthalmology,
The University of Auckland

Dr Joyce Mathan and a patient

Keratoconus is a potentially blinding disease of the cornea, the transparent structure of the eye that is in front of the coloured part (iris). International studies showed that keratoconus is more common in Down syndrome, however the literature is sparse. We identified that among 98 athletes with Down syndrome competing at a national level sporting event, 1 in 3 had keratoconus by utilising a screening device. As a result, a large study was launched to characterise the cornea in 190 people with Down syndrome by comprehensive imaging using multiple devices including three-dimensional imaging of the cornea as well as an eye examination. Participants were followed up at three- or six-month intervals for one year. Additionally, a review of clinical records of patients with Down syndrome attending a public ophthalmology tertiary service was conducted to determine the realities of keratoconus presentation and management. Combined, these studies confirmed that keratoconus and severe forms of keratoconus were common in this group. Due to the lack of clinical guidelines for the care of keratoconus in Down syndrome specifically, these studies informed the development of a proposed clinical guideline to enable early detection of keratoconus, appropriate monitoring, and treatment.

FUNDED BY: John and Poppy Stilson Endowment Trust

KELLIHER CHARITABLE TRUST EMERGING RESEARCHER START-UP AWARDS

$30,000 Award 1719001

Dr Sarah Stewart

Dept. of Medicine,
The University of Auckland

Research support for her Postdoctoral Fellowship titled 'Ultrasound in asymptomatic hyperuricemia'

FUNDED BY: Kelliher Charitable Trust

Kelliher Charitable Trust

Grants Completed continued

SIR DOUGLAS ROBB MEMORIAL FUND

$2,000 Award 1720004

Dr Melissa Cadelis

School of Chemical Sciences,
The University of Auckland

The Sir Douglas Robb Memorial Fund provided me the opportunity to undertake my first independent research project. Through this fund I was able to pursue my passion of developing bioactive molecules. The aim of the project was to synthesise 10 compounds that were simplified analogues of a bioactive antimicrobial natural product as the synthesis of the natural product in its entirety was deemed laborious and expensive. I was able to successfully synthesize eight out of the 10 targeted compounds, the synthesis of the last two compounds were unsuccessful after multiple attempts. All the synthesized compounds were evaluated for antimicrobial activity against a panel of bacterial and fungal pathogens with a collaborator in Australia. Unfortunately, all compounds showed a loss of MRSA activity to varying degree, previously observed in the natural product. The compounds and the natural product were then evaluated for their antibiotic enhancing activity with a collaborator in France using the antibiotics doxycycline and erythromycine against two bacterial strains. However, all the compounds including the natural product failed to enhance the activity of either antibiotic against both strains. These results indicated that all the components of the natural product were necessary for the observed MRSA activity in the natural product and that this class of compounds were not antibiotic enhancers. Fortunately, recent reports of a related natural product have shown this class of compounds to have IDO1 inhibitory properties which is an enzyme targeted in cancer immunotherapy. I now plan on submitting the synthesized analogues for evaluation of IDO1 inhibitory activity to a collaborator at the Auckland Cancer Society Research Centre.

$1,875 Award 1720003

Dr Eryn Kwon

Auckland Bioengineering Institute,
The University of Auckland

The brain is the most complex organ in our body, without easy access for examination. Subtle abnormality of the brain is difficult to visualise non-invasively, and may cause patients to miss out the early treatment for brain injury/diseases such as concussion. A new way of analysing the mechanical properties of the brain using small heartbeat-induced movements, called amplified-MRI (aMRI), is a promising method to see what cannot be seen using traditional approaches. With these funds, we were able to acquire aMRI scans for two human volunteers (one male and one female), at resting and at an elevated heart rate. The aMRI output revealed that the amplification method resulted in consistent outputs without noticeable imaging artefacts. While the sample number is not sufficient to establish any statistical analysis, these preliminary data serve as proof-of-concept in recruiting a larger number of individuals, in order to separate the contributions from cardiac cycle within an individual, and also between individuals. Once our group has conducted further research and recruited more volunteers, these data will establish a healthy baseline for the aMRI, to further refine the technique and make the sequence viable as a routine clinical scan.

HEALTHEX EMERGING RESEARCHER AWARDS

$3,000 - 6718002

Farha Ramzan

Liggins Institute,
The University of Auckland

AMRF Outstanding Emerging Researcher Award: Comprehensive profiling of the circulatory miRNAome response to a high protein diet in elderly men

FUNDED BY: AC Horton Estate

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2021 ANNUAL RESEARCH AWARDS

Donors, stakeholders, partners and family members joined us online in recognising our scholars, fellows and special award recipients.

Prof Dame Juliet Gerrard
Photo credit Elise Manahan

Dr Rachel Taylor

The 2021 Research Awards recognised our scholars, fellows and special award recipients and celebrated the breakthroughs they are making in medical and health science. We heard from both the Prime Minister's Chief Science Advisor, Prof Dame Juliet Gerrard, and Dr Rachael Taylor, AMRF's Edith C. Coan Postdoctoral Fellow.

It was also the opportunity to revisit the Futures Fellowship Fund – our special initiative designed to sustain our mid-career researchers at a critical point in their career. The Futures Fellowship Fund was launched in late 2019 to help researchers in a mid-career phase, attempting to secure an academic position – a position that can provide some sort of security but these are far and few between – while maintaining a rigorous research regime.

To receive a link to the 2021 Research Awards video or find out more about the Futures Fellowship Fund and how you can help, please contact Sue Brewster, Executive Director on 09 923 1701 or email Sue.Brewster@medicalresearch.org.nz.

THANK YOU

James Mutch
Elizabeth Jollands
Noel and Heather Davies
Estate of Margaret Collings
Aotea Holdings Group Ltd
Brenda Shenken
The Taylor Family Trust
Anonymous (2)

Financial Highlights 2021

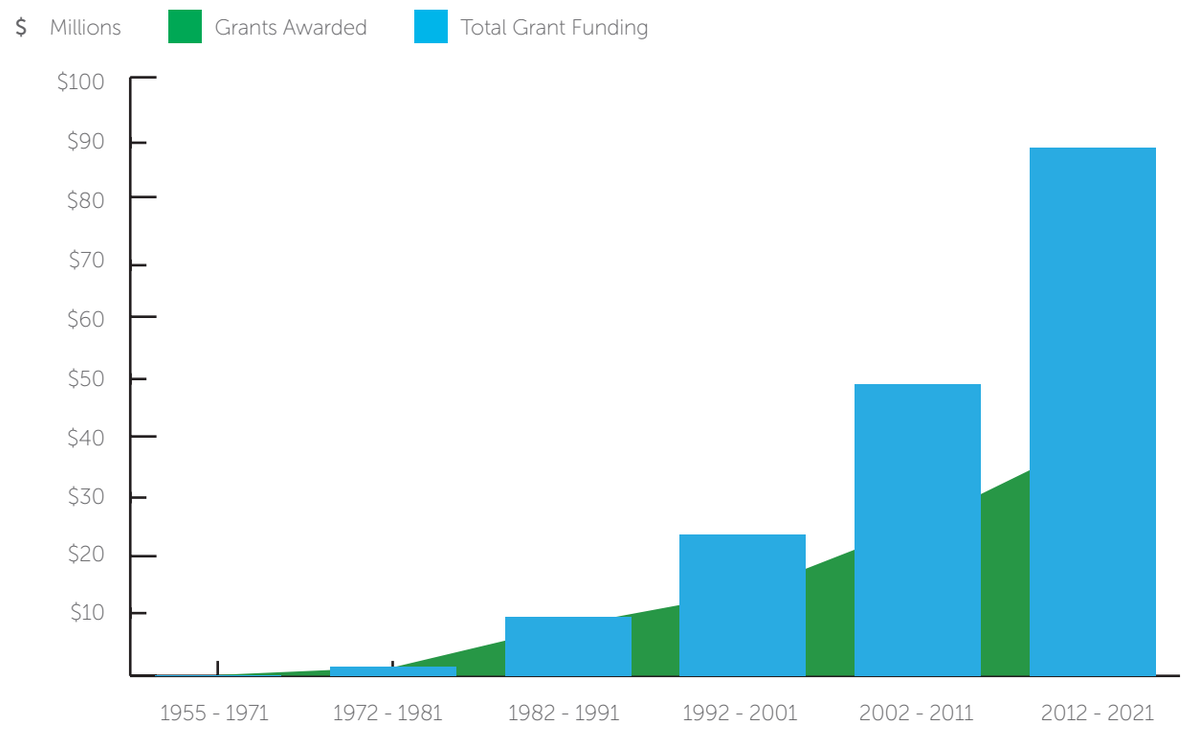
RESEARCH FUNDING 2021 $4.25MILLION TOTAL RESEARCH FUNDING SINCE 1955 $88.3 MILLION

FINANCIAL PERFORMANCE

	Note	2021 $		2020 $	
Revenue					
Donations/Research Income	1	1,511,544		3,341,025	
Investment Income (Total Return)	2	8,068,578		1,969,119	
Other Comprehensive Revenue / (Expense)	1	1,205,096		1,074,572	
Total		**10,785,218**		**6,384,716**	
Expenditure					
Operational expenses		535,657		565,070	
(Less Donation)	3	(535,657)	-	(565,070)	-
Net Research Grant Expenditure	4	4,027,862		4,615,369	
Net Surplus / (Deficit)		**6,757,356**		**1,769,347**	
Trust Equity		**70,490,791**		**63,733,435**	

The summary financial highlights above have been extracted from the Audited Financial Statements which can be obtained by contacting the Foundation's office, or via Charities Services www.charities.govt.nz

AMRF GRANT FUNDING 1955 - 2021



Notes to the 2021 Financial Report

1. Donation & Research Income includes grants, donations (general and specific use), trust distributions and external funding received from the following organisations:

Perpetual Guardian Administered Funds	
The Edith C Coan Trust	120,000
TM Hosking Trust	10,000
John A Jarrett Trust	40,000
C E Lawford Estate	2,940
Rose Richardson Estate & Trust	34,265
Ruth Spencer Estate	300,000
The John & Poppy Stilson Endowment Trust	95,000
N R Thomson Charitable Trust	20,000
The Peter and Jenny Vincent Trust	4,890
The Room Simmonds Charitable Trust	20,000

Public Trust Administered Funds	
The Audrey Simpson Trust Fund	8,000
Ralph Dingle Trust	3,500
Pauline Gapper Charitable Trust	6,600
The Reed Charitable Trust	8,000
The Acorn Charitable Trust	5,750

Other Trusts/Funds	
Anonymous	300,000
Douglas Goodfellow Charitable Trust	457,591
Gooduck Charitable Trust	111,000
The JI Sutherland Fund	75,000
The Kelliher Charitable Trust	44,769
Marion Ross Memorial Fund	83,103
Norah Hamblin Trust	50,000
Paul Stevenson Memorial Trust	25,000

Other Comprehensive Revenue including: Legacies, Bequests and Capital Gifts

Anonymous	Jeff and Glenys Todd
Est of Jean Grinter	Aotea Group Holdings Ltd
Est of Stuart Ross Mackay	Taylor Family Trust
Est of Elaine M Robinson	James Mutch
Hugo Charitable Trust	

2. Investment Income (Total Return)

Following the 2019 switch to managed funds, investment income is recorded on a Total Return basis, whereby all direct income (interest and dividends) and annual portfolio gains or losses are recorded via the Statement of Financial Performance.

3. Operational Expenses

The Foundation is grateful to the Harry, Hector, Douglas, and TB Goodfellow Funds for the ongoing funding of operational expenses.

4. Research Funding Awarded 2021

PROJECT GRANTS (18)	2,407,864
POSTDOCTORAL FELLOWSHIPS (2)	415,874
DOCTORAL SCHOLARSHIPS (3)	393,000
AMRF TRAVEL GRANTS (10)	12,033
OTHER GRANTS	
UoA / AMRF Senior Research Fellowship	100,000
Douglas Goodfellow Medical Research Fellowship	104,000
Douglas Goodfellow Repatriation Fellowship	407,591
Ruth Spencer Medical Research Fellowship	302,000
Kelliher Charitable Trust Emerging Researcher Start-up Grant (2)	44,769
Sir Harcourt Caughey Award	49,971
HealtheX Emerging Research Awards (3)	7,000
Summit Award	3,000
WDHB Award	1,000
TOTAL GRANT FUNDING 2021	4,248,102
Less amounts allocated but not required	(220,240)
NET GRANT EXPENDITURE 2021	**4,027,862**

Special Acknowledgements

WE ARE MOST GRATEFUL TO ALL THE INDIVIDUALS, TRUSTS AND ORGANISATIONS LISTED

Honorary Life Members

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Thanks also to our benefactors who wish to remain anonymous.

BELOW WHO HAVE GIVEN GENEROUS SUPPORT TO THE FOUNDATION DURING THE YEAR.

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Our volunteer Board of Trustees provide a critical governance function to ensure we meet the ever-increasing range of legislative and charitable requirements within our sector. The wide-ranging skill set and expertise of our Board members results in the setting of gold-standard policies and procedures. Their steadfast focus on strategic priorities is the backbone of our ongoing achievement of the AMRF mission but also supports us to respond to the dynamic needs of our research community, particularly over the last two years of the pandemic.

Our AMRF Trust Deed allows for no less than six and no more than 15 Trustees to be appointed and we have been very fortunate to have had an average of 10 highly engaged Trustees on the Board over the last 10 years or so.

In 2021, we farewelled and thanked Christine Ding for her wonderful service to the Board and welcomed two new Board members, Dr Anna King and Katie Noble. You can read more about all of our Board members on our website, www. medicalresearch.org.nz.

Dr Anna King

Dr Anna King is a clinical nurse, with over a decade of experience in academic research and lecturing at The University of Auckland. Her expertise includes clinical skills teaching and older person's health and she has published widely in the field of gerontology. As a board member of the Goodfellow Foundation, Anna supports the Goodfellow Unit's educational and development programmes for primary healthcare professionals. She is Portfolio Manager - Practice Services at ProCare, an Auckland health care cooperative. She joined the board of AMRF in September 2021 and brings a range of skills and experience to help advance the AMRF vision of improving the health and quality of life for all New Zealanders.

Katie Noble

Katie Noble is the Managing Director of Allied Medical Limited providing assistive technology and rehabilitation equipment to New Zealand. She has held additional governance roles in commercial, government and non-profit organisations, including Yes Disability Resource Centre Trust, Make-a-Wish New Zealand, Muscular Dystrophy Northern, Lotteries Auckland Community Distribution Committee and Sunderland School Property Ltd. She joined the board of AMRF in September 2021. With her energetic style of leadership, Katie contributes her expertise in organisational culture, people and sales and marketing to help make New Zealand a better place for us all, no matter what our background or ability.

How You Can Help To Change Lives

HELEN GOODWIN IS FOUNDER AND TRUSTEE OF THE GOODUCK CHARITABLE TRUST AND SHARED HER STORY ON THE IMPORTANCE OF SUPPORTING OUR YOUNG RESEARCHERS.

"When I retired I looked back on a long teaching career and realised how fortunate I had been by people encouraging and supporting me over many years. I wanted to give back to society so set up a charitable trust. One of the aims of the Trust included funds by way of a scholarship. We discovered the wonderful work being done by the Auckland Medical Research Foundation (AMRF) and so in 2018, we awarded a doctoral scholarship to Zoe Woolf for her research into aggresive brain tumours. This was important to me as my partner had died of a brain tumour and, in fact, I also have a non-malignant tumour.

"Following Zoe's three year term, we were then pleased to award a doctoral scholarship to Conor Nelson. Unfortuantely I have not been able to meet with Conor yet because of Covid lockdowns but I hope in the near future we will be able meet up and hear about his research.

"We have appreciated the positive feedback we have received from AMRF and the recipients over the years. I know the importance of these grants to our young gruaduates as they continue with their research. My desire and hope for the future is that my association with the AMRF will continue for many years ahead. We are hoping to award a third scholarship towards the end of 2022."

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Email us at amrf@medicalresearch.org.nz

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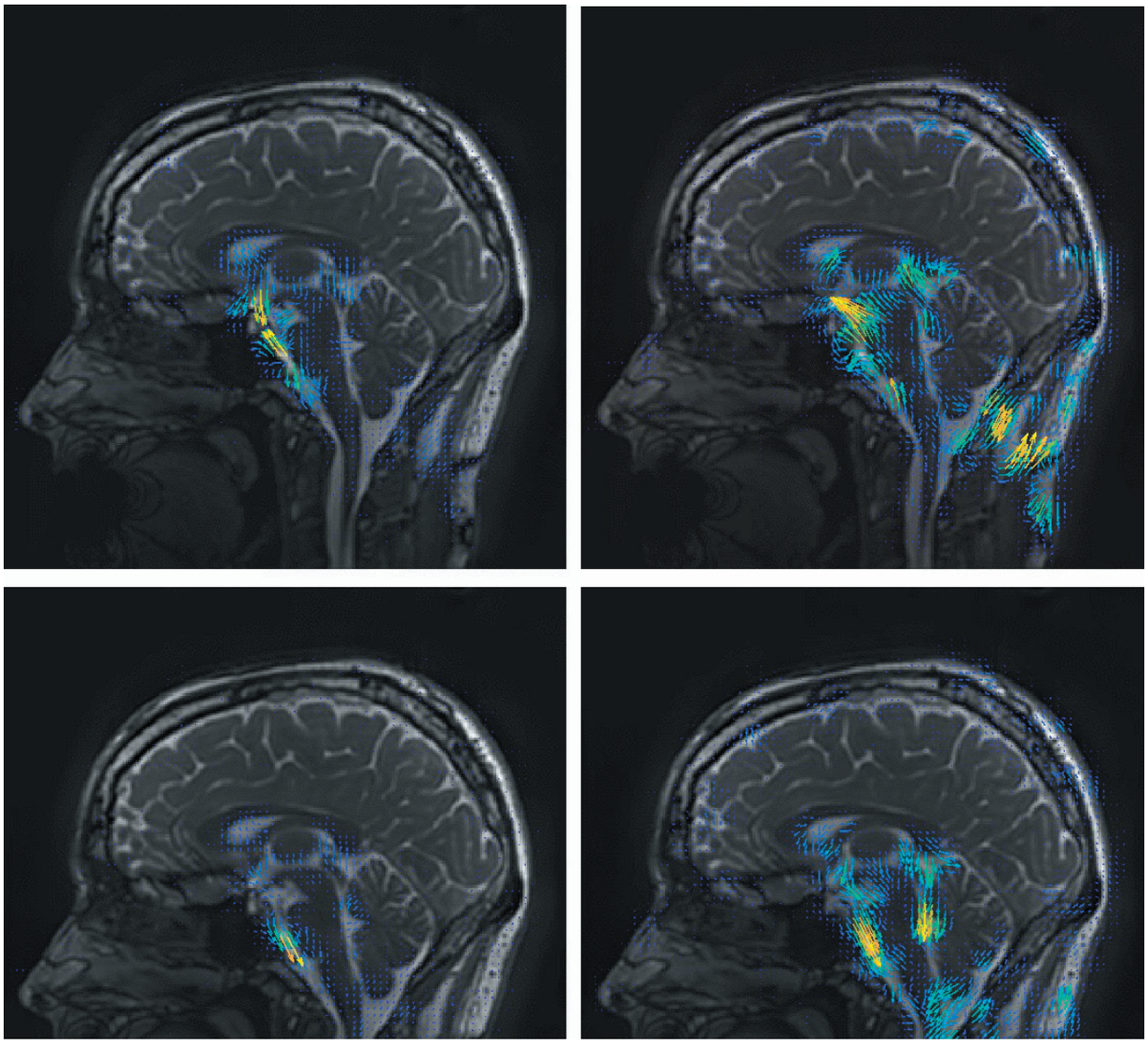
AMRF thanks BlueStar Group for ten years of pro bono design and print of the AMRF annual report and newsletters.



BETTER MRI IMAGING AT HIGH HEART RATES

What is the influence of heart rate on magnetic resonance imaging (MRI) of the brain?

With an elevated heart rate, hydraulic shock to vessels is increased, leading to higher impedance from the brain, negatively affecting imaging. The ability to separate the contributions from the cardiac cycle will enable us to better discern and diagnose different physiological states.

Through the Sir Douglas Robb Memorial fund, Dr Eryn Kwon and collaborators were able to acquire and compare amplified MRI (aMRI) scans at resting and elevated heart rates for proof-of-concept of this technique. They found they were able to compensate for the additional brain motion seen in MRI caused by increased heart rate.

From this preliminary funding, they can now expand their studies to further refine the technique and make the sequence viable as a routine clinical scan. As this is a post-processing technique, it is easily accessible for the general public and will improve diagnosis of neurological diseases, which is a significant health concern not just in New Zealand but worldwide.

This image shows the optical flow (vector arrows showing magnitude and direction of the relative movement of the brain) of a male volunteer baseline aMRI.

Read more on page 28.

Image: Dr Eryn Kwon

Auckland Medical Research Foundation

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