Auckland Medical Research Foundation

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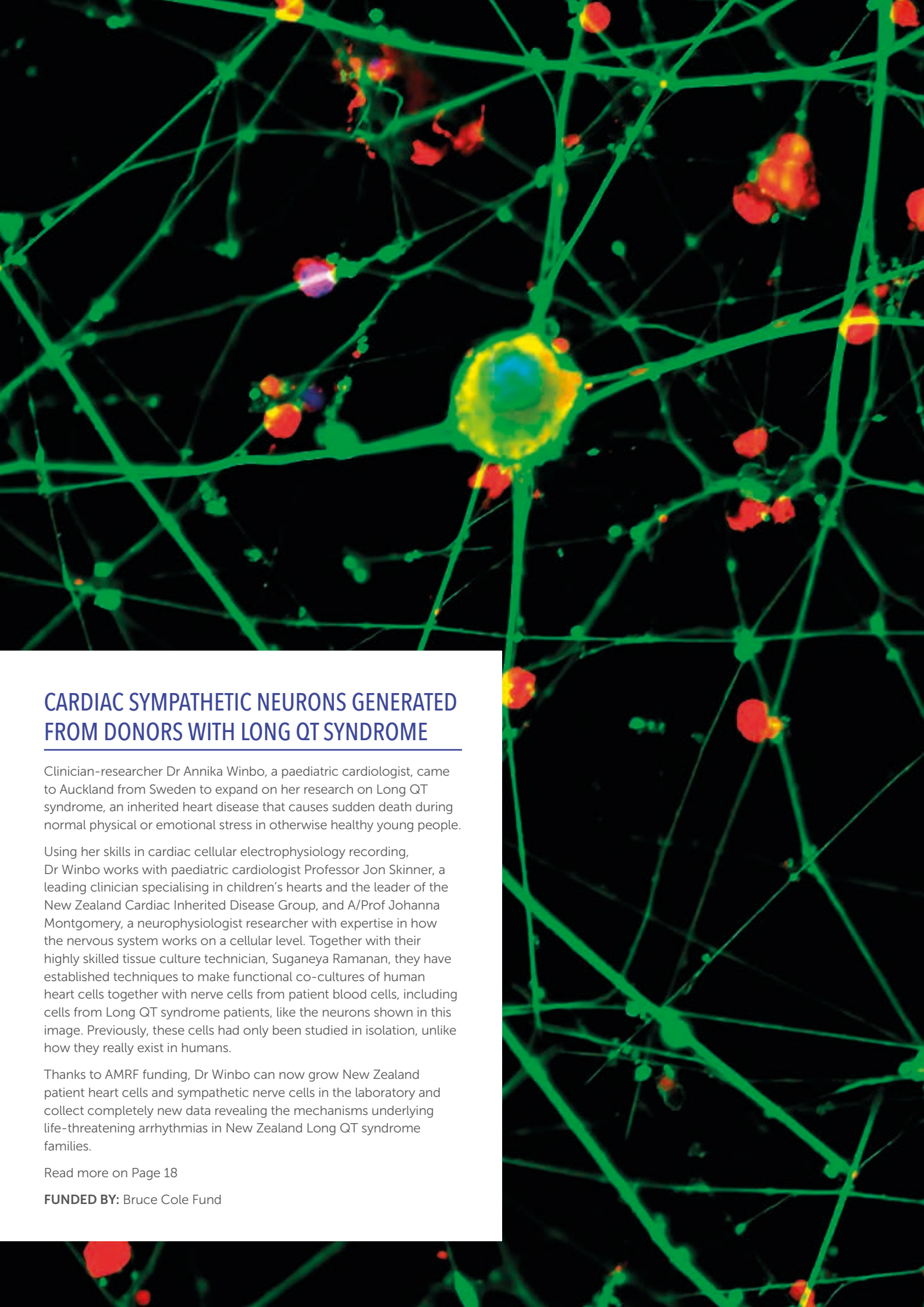
ANNUAL REPORT 2019

SUPPORTING MEDICAL RESEARCH FOR OVER *60 years*



CARDIAC SYMPATHETIC NEURONS GENERATED FROM DONORS WITH LONG QT SYNDROME

Clinician-researcher Dr Annika Winbo, a paediatric cardiologist, came to Auckland from Sweden to expand on her research on Long QT syndrome, an inherited heart disease that causes sudden death during normal physical or emotional stress in otherwise healthy young people.

Using her skills in cardiac cellular electrophysiology recording, Dr Winbo works with paediatric cardiologist Professor Jon Skinner, a leading clinician specialising in children's hearts and the leader of the New Zealand Cardiac Inherited Disease Group, and A/Prof Johanna Montgomery, a neurophysiologist researcher with expertise in how the nervous system works on a cellular level. Together with their highly skilled tissue culture technician, Suganeya Ramanan, they have established techniques to make functional co-cultures of human heart cells together with nerve cells from patient blood cells, including cells from Long QT syndrome patients, like the neurons shown in this image. Previously, these cells had only been studied in isolation, unlike how they really exist in humans.

Thanks to AMRF funding, Dr Winbo can now grow New Zealand patient heart cells and sympathetic nerve cells in the laboratory and collect completely new data revealing the mechanisms underlying life-threatening arrhythmias in New Zealand Long QT syndrome families.

Read more on Page 18

FUNDED BY: Bruce Cole Fund

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Charity Services Registration Number: CC22674

PRESIDENT'S REPORT 2019

"2019 was another successful year for AMRF. On the cusp of our 65th year anniversary, I want to acknowledge all of our incredible supporters who have contributed so that nearly $80 million has been awarded to medical research since 1955."

2019 was also a year that heralded the start of the biggest health crisis experienced in modern day history as the Covid-19 pandemic unfolded.

The rapid escalation and global lockdowns did not fully impact New Zealand until early 2020 but the devastation it left in its wake has changed many lives forever. Aligned to our mission, an AMRF Covid-19 Special Research fund was launched and applications were fast-tracked in response to our research community need. This fund and the resulting research projects will be reported on in our 2020 Annual Report.

The financial performance for 2019 is featured on page 40 along with narrative explaining year-on-year variances in our levels of income and grants awarded. The research income difference is predominantly due to funds received from externally managed trusts in 2018 only being available for distribution every two to three years. This variance is reflected in both the income and research grant expenditure figures for 2019. The variation in investment income is largely due to a strategic decision by the Board to move our investment portfolio from individual securities to managed funds. This change helps future proof our long-term capital, along with the associated income for research grants. Investment income is now calculated on a Total Return basis.

AMRF continues to be the largest independent funder of medical research in New Zealand and this report features the work of world-class researchers who have been awarded this funding. Their research is only made possible by you, our supporters, and it is through your generosity that research in New Zealand continues to find solutions for all types of diseases and conditions, and continues to be transformational in the quality of life of so many.

The story of Dr Tim Angeli on page 4 is one that brings to life the way your support has built critical research pathways for our emerging researchers. Dr Angeli was provided with an AMRF postdoctoral fellowship back in 2016, closely followed by the Kelliher Charitable Trust Emerging Researcher Start-Up Award in 2017. These awards allowed this talented young doctor to progress important research into gastrointestinal disorders along with his own professional development. In 2018, Dr Angeli was granted a five year Rutherford Discovery Fellowship. Through your support, the Dr Angelis of this world will continue to thrive and it is heart-warming to know that Tim is now reciprocating this generosity as a volunteer member of the AMRF Medical Committee.

Behind the scenes, there is a well-oiled machine that ensures the smooth running of the Foundation. I extend my sincere gratitude to our Executive Director, Sue Brewster, and her tremendous hard working team at the AMRF for their professionalism and passion.

To the AMRF trustees, committee chairs and committee members, thank you for your generous donation of time and expert knowledge and the ongoing commitment you have to the achievement of our AMRF mission.

My final thank you is to the Goodfellow family and their associated charitable trusts which fund all of AMRF's operational expenses. This support means that AMRF is in the very unique position of delivering every single dollar of your donation directly into research – research that grows hope, finds new cures and advances medical treatments that will change people's lives forever.

Richard Taylor
President

MEDICAL COMMITTEE REPORT 2019

Covering five grant rounds during 2019, the dedicated Medical Committee worked voluntarily to assess 163 applications, of which 55 grants were awarded totalling $3.4 million.

High levels of demand for research funding continue in this competitive space, so the AMRF board were pleased to award 34% of the total funding requested through 2019 grant applications. This percentage is amongst the highest of funding ratios in the arena of medical and health research funding in New Zealand.

Particular highlights were the awarding of three Doctoral Scholarships, one Postdoctoral Fellowship and a one year extension to the Douglas Goodfellow Repatriation Fellowship, highlighting the AMRF's role in supporting young and emerging researchers. Another highlight was the continued relationship with the Kelliher Charitable Trust with the awarding of the 2019 Kelliher Charitable Trust Emerging Researcher Start-up Awards for our Postdoctoral Fellows from the previous year. The support from our valued donors and members also enabled crucial grant funding for 19 projects covering a multitude of themes, examples of which include mental health, cochlear biology, cardiac arrhythmias and drug development. All of the 2019 funded grants demonstrate the breadth and depth of the excellent research being undertaken in the Auckland and Northland regions.

The awarding of these grants would not be possible without the generous gifting of time and expertise of our Medical Committee members who, as always, ensured a contestable and robust assessment process was followed for all of the applications. In 2019, we welcomed to our committee as full members Dr Tim Angeli from Auckland Bioengineering Institute, and Associate Professor Srdjan Vlajkovic and Dr Julie Lim from the Department of Physiology, The University of Auckland. Their level of expertise and new insights will continue to guarantee the very highest standard of review process being undertaken by our committee.

On behalf of the Medical Committee, I would like to thank the AMRF team, expertly led by Sue Brewster, for the administration and background work that goes into our funding processes. 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. I would also like to thank our Board of Trustees, under the superb 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.

It would be remiss of me to finish this report without mention of the coronavirus pandemic which hit the world headlines in December 2019. While New Zealand was able to mitigate the catastrophic loss of life that was seen in so many other countries, I would like to acknowledge the economic impact and very significant financial challenges we will face as a nation and within our research community. Our focus, more than ever, needs to be on research as the provider of solutions and answers for future health crises along with improving treatments and finding cures for all diseases and medical conditions.

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

PROVIDING ANSWERS FOR UNEXPLAINED STOMACH DISORDERS

Dr Tim Angeli

Auckland Bioengineering Institute

When Dr Tim Angeli reflected on his pathway to developing new and minimally-invasive ways of diagnosing digestive disorders, he knew he had AMRF donors to thank for helping him on his path. Tim was the recipient of the 2016 Edith C. Coan Postdoctoral Fellowship and, in 2017, received one of two Kelliher Charitable Trust Emerging Researcher Start-up Awards.

In a rare feat for such a young researcher, charitable giving enabled Tim to bring his promising endoscopic gastric mapping technology into the clinic as a new diagnostic tool to help patients with unexplained GI distress.

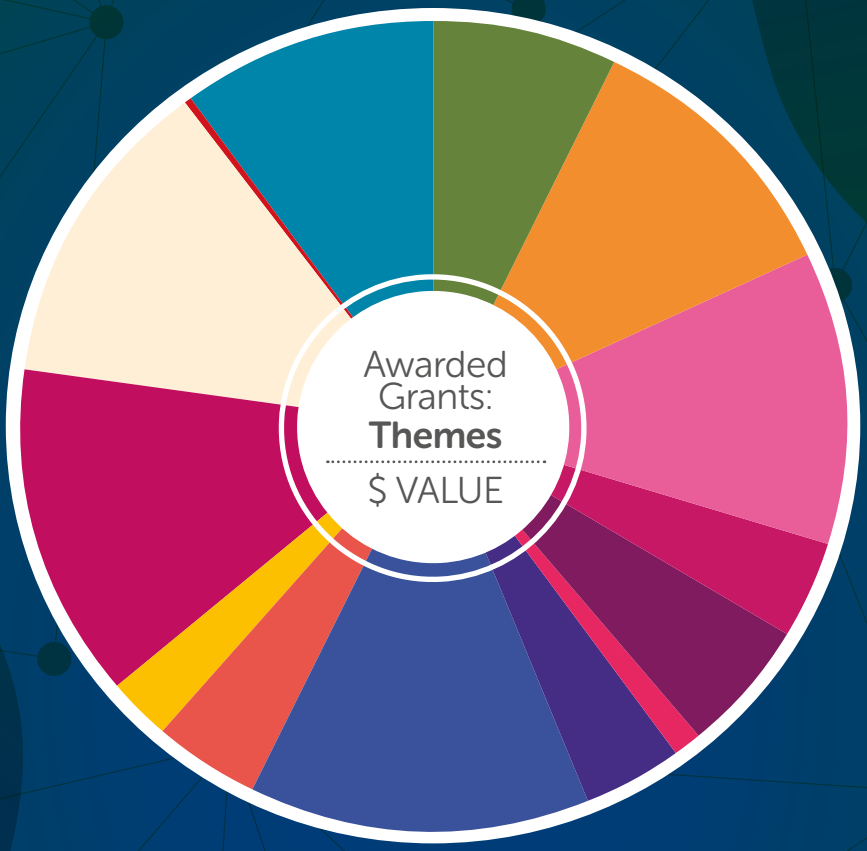
In late 2018, and in recognition of his ground-breaking research, Tim has been awarded a prestigious Rutherford Discovery Fellowship to ensure he can keep focusing on the urgent need for new diagnostic and therapeutic strategies to address GI disorders. The next steps for Tim include establishing a dedicated research lab in this field, the Laboratory for TrAnslational Research in Gastroenterology and Emerging Technologies (TARGET Lab). This group will contribute a new generation of minimally-invasive, electrophysiologically-based diagnostic and therapies for GI disorders, aiming to bring relief to thousands in New Zealand and around the world.

In 2019, AMRF began to receive the benefit of Tim's expertise as he became a valued member of the Medical Committee, reviewing applications and recommending research projects for funding.

Tim says, "My next career stage will be built upon the work that I was able to do with the support of an AMRF Fellowship and was greatly helped by the generous funding that the Kelliher Charitable Trust provided. I'm extremely grateful to the charitable donors who have made this work possible, and I hope they, and their loved ones, will benefit from my work."

"This funding was a true enabler for my research and allowed me to conduct experiments and trials that resulted in the development of a safe and effective technique - endoscopic gastric electrical mapping - along with supporting the very important, next phase of translation of this technique to human trials", he says. "Helping real people with my work has always been the goal for me."

GRANTS AWARDED



2019 AWARDED GRANTS – THEMES
55 GRANTS AWARDED TOTALLING $3,376,920

- Biomedical Imaging (4) | **$249,550** | 7.4%
- Cancer (7) | **$364,327** | 10.8%
- Cardiovascular Science (4) | **$398,471** | 11.8%
- Cellular and Molecular Biology (3) | **$122,797** | 3.6%
- Endocrinology, Metabolism and Nutrition (4) | **$181,787** | 5.4%
- Infection and Immunity (5) | **$37,427** | 1.1%
- Musculo-skeletal Science (3) | **$133,000** | 3.9%
- Neuroscience (6) | **$453,653** | 13.4%
- Other (3) | **$136,670** | 4.0%
- Population Health (3) | **$85,619** | 2.5%
- Reproduction, Development, Maternal and Newborn Health (5) | **$446,594** | 13.2%
- Sensory Sciences (4) | **$427,241** | 12.7%
- Stem Cell Biology (1) | **$2,652** | 0.1%
- Surgery (3) | **$337,132** | 10.0%

$ Value each theme
(n) Number of grants

% Total expenditure

POSTDOCTORAL FELLOWSHIP

EDITH C. COAN POSTDOCTORAL FELLOWSHIP

PROBING THE BIOCHEMISTRY OF SKIN WITH LASERS, LIGHT SCATTERING AND MOLECULAR IONISATION ($200,306 - 2 years) 1319001

Dr Hannah Holtkamp

School of Chemical Sciences,
The University of Auckland

Diagnosing different skin diseases is dependent on an instrument's ability to identify the unique signals of each disease. Unstudied skin diseases have ill-defined biochemistry and require analytical techniques that can provide a broad biomolecular survey. Two techniques are capable of this, and they generate two different spectral fingerprints. Raman spectroscopy is non-invasive (making it ideal for diagnostics) and provides a precise ratio of biomolecular components present in tissue (e.g. lipids, proteins, etc). Mass spectrometry (MS) is invasive but identifies all individual biomolecules present by their mass-to-charge (m/z) ratio. By developing computational algorithms, the precise molecular information from mass spectrometry can be incorporated into Raman measurements with which the unique aspects of any skin disease can be more precisely identified. Discoid lupus erythematosus (DLE) is a case study for these techniques due to its distinctiveness compared to other types of lupus. Unless one is an expert dermatologist, its classification and diagnosis are challenging. This project will contribute to a fundamental understanding of how DLE differs from other skin diseases. Furthermore, the computational methods that provide enhanced dermatological diagnostic resolution will be incorporated into the development of a Raman spectroscopy-based portable device (currently under development).

Read more on page 18.

FUNDED BY: Edith C. Coan Trust

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DOCTORAL SCHOLARSHIPS

EDITH ROSE ISAACS DOCTORAL SCHOLARSHIP

PLATELET-DERIVED GROWTH FACTOR SIGNALLING IN PATIENT-DERIVED BRAIN CELLS ($128,000 - 3 years) 1219004

Susan Li

Dept. of Pharmacology & Clinical Pharmacology,
The University of Auckland

Platelet-derived growth factor (PDGF) is a potent mitogen involved in the proliferation, migration and survival of cells, with its effect mediated via the activation of its receptors, PDGFRα and PDGFRβ, and subsequent signalling pathway. Studies have revealed evidence of its involvement in the maintenance of blood-brain barrier integrity by promoting proliferation and survival of pericytes, a mural cell type critical to vascular function. The PDGF receptors are also found in glioma cells, playing a role in tumour development and progression, especially in Glioblastoma Multiforme (GBM), the most common and malignant primary brain tumour. Preliminary data from our lab show that both pericytes and glioma cells abundantly express the PDGF receptors and have distinct signalling properties. This project aims to thoroughly characterise the PDGF signalling pathway, with emphasis on brain pericytes and GBM glioma cells.

FUNDED BY: The Edith Rose Isaacs Estate

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AMRF DOCTORAL SCHOLARSHIPS

RURAL: REGIONAL VS URBAN RISK OF APPENDICITIS COMPLICATIONS ($18,000 - 1 year) 1218003

Dr Brodie Elliot

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

Appendicitis is the most common and costly emergency general surgical disease that affects children. International studies have shown that rural patients are more likely to have poorer outcomes of appendicitis. This results in distress and harm for children and their families in the form of pain, increased stay in hospital, and need for repeat invasive procedures. Despite a quarter of New Zealanders living in a rural or small centres, no study has investigated whether this problem exists here. We will first interview the families of children who have undergone an emergency appendicectomy and study any common themes that prevent rural families from accessing surgical care. Using this information we will then investigate the presentation and outcomes of all children who undergo surgery for appendicitis, nationally. This research will be used to identify any common barriers faced by rural families in accessing acute paediatric surgical care and whether surgical outcomes of appendicitis are worse for children of rural families on a national scale. This will act as a platform to guide public health improvement efforts, improve rural access to healthcare and reduce the impact of this common disease on the New Zealand's children.

FUNDED BY: Curtis-Tonkin Paediatric Fund

TROPHOBLAST STEM CELLS AND FETAL GROWTH RESTRICTION ($128,000 - 3 years) 1219006

Cherry Sun

Dept. of Obstetrics & Gynaecology,
The University of Auckland

The placenta mediates nutrient exchange between mum and baby, and its ability to do this depends on specialised placental cells called trophoblasts. Aberrant placentation and trophoblast differentiation/function are major contributors to diseases of pregnancy such as fetal growth restriction (FGR). FGR remains an important problem it has no effective treatment, in part because we do not understand why it occurs. The James lab has developed a new method to isolate trophoblast stem cells (TSC, from which all mature trophoblasts arise) directly from the placenta without culture, and this has allowed the isolation of TSCs from term placentae for the first time. This is critical to understand how TSCs contribute to pregnancy pathologies, which can only be detected clinically in late pregnancy. Isolating TSCs from normal and FGR placentae has revealed that this population are significantly (10-fold) depleted in FGR placentae, and gene expression studies suggest this is a result of reduced cell proliferation and increased cell death. This project aims to understand how functional differences in the proliferation, death, and differentiation of TSCs may contribute to the pathophysiology of FGR. This will allow us to identify potential therapeutic targets to improve the function of FGR placentae in the future.

FUNDING CONTRIBUTION BY: John Jarrett Trust

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AMRF SUPPORTS THE WAITEMATĀ DHB HEALTH EXCELLENCE AWARDS

DR JACQUELINE ALLEN

Otolaryngology, North Shore Hospital, Waitematā District Health Board

$500 TRAVEL AWARD 6719005

Best Oral Presentation (Research) Award at the 2019 Waitematā DHB Health Excellence Awards: The real costs of swallowing complaints in a public health system.

Difficulty swallowing (dysphagia) may lead to aspiration pneumonia and death. In a hospital setting where patients are admitted for other causes (in this case, hip fracture), a complaint of dysphagia, in addition to hip fracture, lengthens inpatient stays and cost per patient. Dysphagia screening at admission to hospital allows early identification of swallow compromise and may prevent complications and reduce costs.

MR DANIEL WEN

School of Medical Sciences, The University of Auckland

$500 TRAVEL AWARD 6719006

Emerging Researcher Award at the 2019 Waitematā DHB Health Excellence Awards: WDHB Skin Service: GP Surgeon Scheme (GPSI), an effective model of care.

Waitematā District Health Board has implemented a new approach to management of skin cancers by triaging lesions to specialist-trained general practitioners with the aim of reducing patient wait times and treatment costs. Daniel's study validates the use of general practice surgeons and shows their integral role in managing the enormous volume of skin cancer in New Zealand.

SUMMIT POSTDOCTORAL RESEARCH PRESENTATION AWARD

DR CAROLINE WALKER

Centre for Longitudinal Research,
The University of Auckland

$3,000 TRAVEL AWARD 6719001

To attend a conference to present her research titled 'Association between maternal depression symptoms and child telomere length: Evidence from Growing Up in New Zealand.'

HEALTHEX EMERGING RESEARCHER AWARDS

MISS PANIA BRIDGE-COMER

Liggins Institute,
The University of Auckland

$3,000 TRAVEL AWARD
6719002

To attend the 67th Annual Meeting of the Society for Reproductive Investigation (SRI) in Vancouver, Canada, 10 – 14 March 2020.

FUNDED BY: Wellington Sisters Charitable Trust

MISS ALANA WHITCOMBE

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

$2,000 TRAVEL AWARD
6719003

To attend a conference to present her research in the field of infection and immunity.

FUNDED BY: Wellington Sisters Charitable Trust

MISS MOLLY ABRAHAM

Dept. of Physiology,
The University of Auckland

$2,000 TRAVEL AWARD
6719004

To attend the FENS 2020 conference in Glasgow, Scotland, 11 - 15 July 2020.

Grants Awarded

PROJECTS

MASTERSTROKE ($159,950 – 2 years) 2119013

Dr Doug Campbell, Prof Tim Short, Dr Carolyn Deng, Prof Alan Barber, Prof Chris Frampton

Department of Anaesthesia, Auckland District Health Board

Dr Doug Campbell

Stroke is the third most common cause of death in New Zealand and is one of the leading causes of long-term disability at all ages. A life-saving clot retrieval procedure can save the lives of patients who get to hospital within the first six hours of having an ischaemic stroke (caused by a blood clot). The clot can be removed using a mesh like retrieval device, freeing the clot from the brain. Getting a patient to hospital quickly following symptoms of a stroke can be life-saving with longer delays indicating poorer outcomes. In New Zealand, 90% of clot retrieval procedures are performed under general anaesthesia. Under anaesthesia during stroke, blood pressure (BP) management is critical. Many anaesthetic drugs can affect the blood flow within the brain. There is a possible mechanism of benefit from an increased BP target. A large randomized control trial is the only way to reliably investigate BP management during clot retrieval and further improve outcomes from stroke.

PLACENTAL TOXIN IN PREECLAMPSIA ($159,998 – 2 years) 1119010

Prof Larry Chamley, Dr Torsten Kleffmann, Dr Carolyn Barrett, A/Prof Katie Groom, Dr Charlotte Oyston

Dept. of Obstetrics & Gynaecology, The University of Auckland

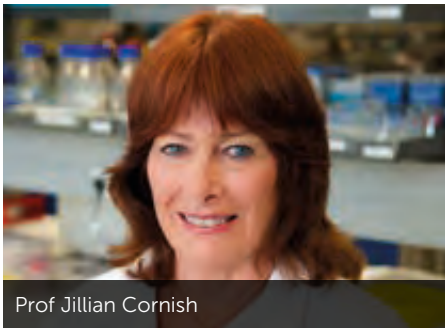
Prof Larry Chamley

Preeclampsia is a disease found only in pregnant women. A woman with a preeclamptic pregnancy has dangerously high blood pressure that results in damage to many of her organs and can potentially cause her death. The only way to prevent this is to deliver the baby, often prematurely with long-term consequences for the baby. Mothers who have preeclamptic pregnancies also have long-term risk of heart disease and stroke. We do not know exactly what causes preeclampsia but we do know that toxins released from the placenta cause damage to mum's blood vessels resulting in high blood pressure/preeclampsia. The nature of the placental toxins is not known, but we have shown that extracellular vesicles, tiny packages from the placenta, are different between preeclamptic and normal placentas and that preeclamptic vesicles are toxic to maternal blood vessels. Extracellular vesicles carry a large number of proteins that could be toxic but only a few of these have been identified. In this project we will use a newly developed technique to characterise all of the proteins in preeclamptic extracellular vesicles to see which are toxic. We will also give preeclamptic vesicles to pregnant mice to confirm that these vesicles cause high blood pressure/preeclampsia.

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

Infection following joint replacement surgery is a devastating complication. It leads to prolonged hospital admissions and poor outcomes for patients and is a heavy economic burden for the health care system. With an aging population and the increased demand for joint replacements, we urgently need to reduce the incidence of infection and improve its treatment. A main challenge of joint replacement infections is the formation of bacterial biofilms on implant surfaces. Once there, the biofilms make the bacteria resistant to antibiotics and the natural defences of the body. This helps the bacteria to gain a foothold in the replaced joint, causing infection that is difficult to eliminate. We have discovered that a novel protein from milk products, lactoferrin, has a natural ability to disrupt bacterial biofilm. This makes them much more susceptible to both antibiotics and the body's natural defences. Our project will evaluate the effectiveness of lactoferrin for both preventing and treating joint replacement infections. This will be done both in our laboratory and in a rat joint replacement infection model. We have an experienced team of orthopaedic surgeons, microbiologists and molecular biologists who can transfer the knowledge gained in our project from the laboratory to the bedside.

ASSESSING METHOD AGREEMENT IN INSULIN QUANTIFICATION BETWEEN BIOVOLT AND AUT ROCHE ($5,480 - 6 months) 5119007

Dr Catherine Crofts, Mrs Marie Mckay, Dr Amira Hassouna

School of Interprofessional Health Studies, Auckland University of Technology

Dr Catherine Crofts

People with high blood insulin levels have a high risk of developing type 2 diabetes, heart disease, certain cancers or dementia. We want to find a simple test for identifying these people and monitoring whether lifestyle changes can keep their blood insulin levels low and decrease their risk of these diseases. We have access to the BioVolt point-of-care device that will measure insulin levels through a fingerstick blood sample. Before we can use this device, we need to first prove that it is as accurate as the normal laboratory testing processes. We are also concerned that insulin levels in capillary (fingerprick) blood may be different to that in the usual sample of venous blood. We plan to compare the insulin levels between venous and fingerstick blood samples on both the BioVolt device and though normal practices. Once tested, we want to use the BioVolt device in both research and clinical practice to help keep people healthy.

COLLAGEN VI KNOCKOUT ($79,593 - 2 years) 1119001

Dr David Crossman, Dr Carolyn Barrett, Prof Christian Soeller, Prof Peter Ruygrok, Prof Bruce Smaill, Dr David Baddeley, Dr Prasanna Kallingappa

Dept. 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 contract. This is a serious health condition and a major cause of death of New Zealanders. Through previous research support from Auckland Medical Research Foundation, we have identified collagen VI is likely responsible for damaging the electrical connections responsible for signalling muscle cell contraction. In this project, we will test if removal of collagen VI can be used to prevent damage to these electrical connections and improve cardiac function after myocardial infarction. This will be done by using our state-of-the-art super-resolution microscope to image, at the nano-scale, the structure of these critical electrical connections.

INVESTIGATION OF LENS PROTEIN FLEXIBILITY ($117,192 – 2 years) 1119018

Dr Nicholas Demarais, Prof Paul Donaldson, Dr Angus Grey, Dr George Guo

School of Biological Sciences, The University of Auckland

Dr Nicholas Demarais

The proteins in the centre of your eye lens have been with you since you were born. Although these proteins are tough, they breakdown and change over their long lifetime. This change is necessary for normal eye function; however, it can also result in negative effects. One such outcome is presbyopia, which is the loss of near vision due to a stiffening of the lens. It is thought to be caused by accumulation of large, inflexible protein assemblies. In most, these collections of proteins are non-hazardous; however, under certain conditions they can cause the eye to become cloudy and form the disease cataract. How these proteins change their structure with age and position in the lens for positive and negative health outcomes is still unknown. Like a topographical map, this work will map the identity and structure of proteins directly from the lens to understand how they change with age and disease state. These results can be used to develop early detection schemes, and to help design the next generation of therapies to alleviate these diseases.

Grants Awarded continued

WHO ARE THE 1M AND 1X? ($79,764 – 1 year) 1119011

A/Prof Daniel Exeter, Dr Katey Thom, Prof Brian McKenna, Dr Anthony O'Brien

Section of Epidemiology & Biostatistics,
The University of Auckland

A/Prof Dan Exeter

Every day, the New Zealand Police (NZP) respond to over 100 calls per day from citizens in distress or the whānau. Indeed, mental health is one of the six major demands on police resources, with approximately 280 hours per day of NZP time spent on mental health-related calls. While a considerable amount of research has been undertaken to understand the needs of citizens with mental health and addiction challenges from a public health perspective, to date no studies have considered these from a policing perspective in New Zealand. This research aims to better understand the socio-demographic context of people in mental distress who have sought support from the NZP between 2013 and 2019, using a whole-of-population cohort created in Statistics New Zealand's Integrated Data Infrastructure (IDI). Importantly, all of our data will be de-identified and we will map the geographic patterns of police responses to mental health/addiction ("1M") or suicidal ("1X") calls. We also explore whether people in mental distress contacting police (1M/1X) have also sought support for their challenges from relevant publically funded health and social support services. Working closely with Māori in this research, we aim to improve the health and wellbeing of the 1M/1X population or the coordination of health and social services for those in mental distress, while striving to address ethnic and social inequities.

THE FIIX STUDY ($152,825 - 2 years) 1119003

Prof Cynthia Farquhar, Dr Sarah Lensen, Dr Lynn Sadler

Dept. of Obstetrics & Gynaecology,
The University of Auckland

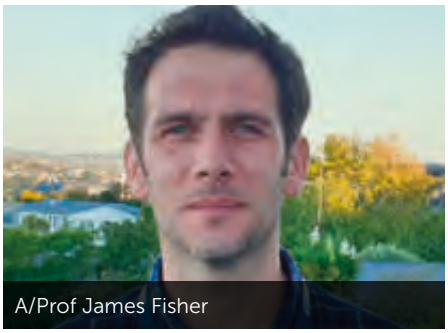
Prof Cynthia Farquhar

One in six New Zealand (NZ) women experience a delay in conceiving. Thirty percent of infertile couples have unexplained infertility. Currently women with unexplained infertility in NZ must have tried to conceive for five years prior to a one year waiting list for in vitro fertilisation (IVF). Our research group has recently reported that 30% of women who have three cycles of intrauterine insemination (IUI) will have a live birth. The public funding in NZ allows women to choose four cycles of IUI or one complete cycle of IVF. This study will provide data comparing four cycles of IUI and one complete cycle of IVF allowing women to be fully informed about the best strategy. We will also be considering the impact of four cycles of IUI on the subsequent two IVF cycles including cost effectiveness. If we are able to report that four cycles of IUI followed by two cycles of IVF is less expensive than two cycles of IVF then it is likely to have a global impact as then IUI can be offered as an first line alternative to IVF. The information from this study has the potential to influence policy and funding for fertility in NZ and beyond.

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



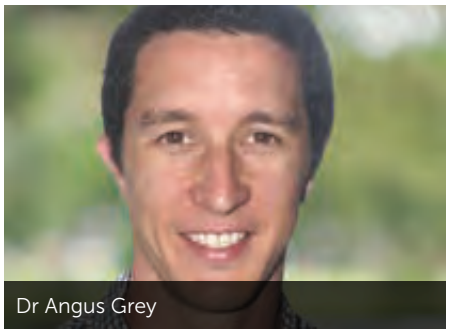
A/Prof James Fisher

One in three New Zealanders have high blood pressure, which can cause stroke, kidney and heart failure. Its asymptomatic characteristic means it can go undetected. More alarming is that half of those patients on medication do not have their blood pressure controlled suggesting that current medications are not effective. The proposed project will establish if the reason blood pressure goes up relates to changes in the detectors of carbon dioxide (CO_2), a product of metabolism, in blood. These detectors are located in the carotid arteries and the brainstem and powerfully increase blood pressure when stimulated. Patients will be recruited from a recently formed high blood pressure network spanning five district health boards. In a brand new specialist Human Research Laboratory within the ADHB, we will determine whether CO_2 detectors are sensitised in people with high blood pressure. We believe they are and that the detectors in the carotid artery are, in part, responsible for the sensitivity of brainstem CO_2 detectors. Our findings may reveal a novel mechanism for why people become hypertensive. This information will be critical for developing new management strategies to control blood pressure using both repurposed drugs and medical devices, which may become available to us in due course.

ANTI-CATARACT NANOVESICLE DEVELOPMENT ($158,539 – 2 years) 1119015

Dr Angus Grey, Prof Paul Donaldson, Dr Ilva Rupenthal, A/Prof Zimei Wu

Dept. of Physiology,
The University of Auckland



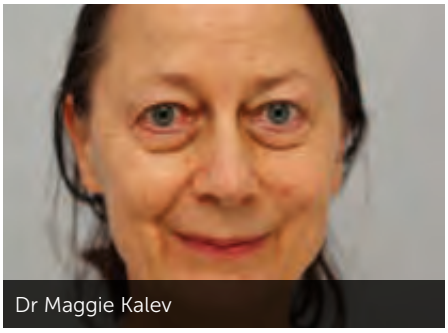
Dr Angus Grey

The number of people afflicted by cataracts is estimated to reach 30 million as the world's population ages. Faced with a looming cataract epidemic, research has focused on developing anti-cataract therapies to prevent cataract and reduce the need for surgery. Since cataract is associated with decreased levels of antioxidants specifically in the lens centre, the use of dietary antioxidant supplements has been advocated as a therapeutic approach to slow cataract progression. However, studies into their efficacy are mixed due to an inability to target their delivery. Our research first addresses a fundamental question on how lens physiology and metabolism maintains tissue transparency, and lays the foundation to then pharmacologically harness lens physiology to deliver therapeutic molecules to specific regions of the aging lens to delay or prevent the onset of lens cataract. First we will assess our ability to pharmacologically stimulate the lens to deliver nutrients to the nucleus, before then packaging therapeutic molecules in nanovesicles to enable their delivery to the lens nucleus. This will determine whether we can enhance the lens antioxidant defence system and prevent or delay the onset of cataract, for which no preventative treatment currently exists.

UPR IN MPN ($159,999 – 2 years) 1119009

Dr Maggie Kalev, Prof Stefan Bohlander, Dr Dean Singleton

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



Dr Maggie Kalev

This work focuses on patients with essential thrombocythaemia (ET) and primary myelofibrosis (PMF). Both are chronic but incurable blood cancers characterised by abnormal platelet counts in the blood and atypical platelet precursors in the bone marrow. While patients with ET have a near-normal life expectancy, survival of patients with PMF is significantly shorter. The reason for the difference is unclear, as both ET and PMF share the same driver mutations. We hypothesise that an adaptive pro-survival response in bone marrow cells determines the disease phenotype. Simply, driver mutations are damaging and cause cell "stress". Cancer cells find ways to counteract the stress by recruiting certain pro-survival mechanisms, which allows driver mutations to cause the disease. As the pro-survival response strengthens, the disease becomes more damaging. We will use bone marrow samples from patients to identify pro-survival mechanisms recruited in ET and PMF. Findings will be correlated with patient diagnosis and driver mutations. Then, small molecules will be chosen to inhibit cell stress response in culture, with an idea that selected molecules may help restrict mutational effects. Our results will provide proof-of-concept evidence that drugs that inhibit cell stress response can help control disease manifestations in patients.

FUNDED BY: Anonymous donor

HYALURONAN SIGNALLING & OGD IN THE DEVELOPING BRAIN ($158,403 - 2 years) 1119005

Dr Rashika Karunasinghe, Dr Justin Dean, Prof Janusz Lipski

Dept. of Physiology,
The University of Auckland

Dr Rashika Karunasinghe

Our ability to form memories and learn is fundamental to the way we experience life. These processes are coordinated by highly-specific and wire-like connections from neuronal cells in the hippocampal region of the brain, which mostly develop before birth and during early childhood. However, these become disrupted in infants diagnosed with brain injury after low oxygen and glucose availability during birth. Survivors show abnormal neuron growth and activity (typified by seizures and learning problems), affecting brain functions throughout later life. However, scientists and clinicians are still challenged by why and how low oxygen and glucose affects neuronal development. We recently found that young neurons produce a key sugar called 'hyaluronan', which normally controls their growth. However, experimentally restricting brain blood flow, and thereby limiting oxygen and glucose supply, caused a loss of brain hyaluronan. We now propose that a loss of hyaluronan causes the abnormal neuronal development in young infants. The main objective of this study is to explore how abnormal levels of hyaluronan may alter hippocampal neuron development following a reduction in the supply of oxygen and glucose to the brain. The ultimate goal is to explore whether hyaluronan can restore brain development in affected infants.

FUNDING CONTRIBUTION BY:
N R Thomson Charitable Trust
perpetual guardian

Grants Awarded continued

MIDODRINE TO PREVENT ORTHOSTATIC INTOLERANCE AFTER HIP AND KNEE JOINT REPLACEMENTS ($159,132 - 2 years) 8119004

Dr Michal Kluger, Ms Monica Skarin, Dr David Rice, Prof Peter McNair

Anaesthesiology and Perioperative Medicine, Waitemata District Health Board

Dr Michal Kluger

After a hip or knee joint replacement it is important to mobilise (get out of bed and move) early to recover faster, and reduce the risk of complications after surgery. Mobilisation can be hindered by orthostatic intolerance, described as the development of symptoms (dizziness, nausea, vomiting, blurred vision, feeling of heat, and fainting) when standing upright. Orthostatic intolerance has been reported to happen in up to 60% of patients after surgery. Reasons include an inability of the peripheral blood vessels to constrict (tighten) properly in response to standing. Midodrine is a drug that works by constricting the peripheral blood vessels, thereby improving blood pressure. This study aims to investigate if midodrine can reduce the occurrence of orthostatic intolerance after hip and knee joint replacements. One hundred and seventy patients will be randomised to receive either midodrine or placebo in the early postoperative period. Orthostatic intolerance will be assessed on the day of surgery, and on the first day after surgery. Midodrine is effective in treating chronic orthostatic intolerance and we believe the administration will reduce the occurrence of orthostatic intolerance in patients after hip and knee joint replacements. This may lead to faster recovery and shorter stay in hospital.

TME STRESS IN HNSCC ($151,615 – 2 years) 1119012

Dr Tet-Woo Lee, Dr Stephen Jamieson, Dr Dean Singleton

Auckland Cancer Society Research Centre, The University of Auckland

Dr Tet-Woo Lee

The microenvironment in which tumours grow is low in oxygen, acidic and deficient in nutrients. Tumours must adapt to these stressful conditions to survive and do so through changes in gene regulation. However, many of the genes responsible for promoting survival of tumour cells within this hostile microenvironment remain unknown. Using a method called a functional genomics screen, we have systematically identified genes in head and neck cancer cells that could modulate tolerance to various microenvironment stressors, including low oxygen, acidic pH and nutrient deprivation. In this project, we plan to validate the findings of our functional genomics screens by individually investigating these identified genes. In doing so, we will improve our understanding of the biology that underpins tumour cell survival in these hostile conditions, as well as uncover potential new targets for therapeutic intervention in head and neck cancer.

FUNDED BY: Anonymous donor

CREBRF VARIANT IN BETA-CELL FUNCTION ($159,324 – 2 years) 1119019

Dr Troy Merry, Dr Paul Docherty, Dist. Prof Geoffrey Chase, Dr Rinki Murphy, Prof Peter Shepherd

Discipline of Nutrition, The University of Auckland

Dr Troy Merry and team

New Zealand's largest and fastest growing health problem is type 2 diabetes (T2D). Elevated blood sugar levels associated with T2D increases the risk of developing many related diseases like cardiovascular disease (CVD), liver disease, stroke and microvascular complications that lead to blindness, amputations and chronic kidney failure. Genetics is a major factor contributing to an individual's risk of developing T2D. Recently a small change in a gene called CREBRF has been shown to be protective against the development of T2D. This genetic variation is present in 20-30% of people of Polynesian ancestry living in New Zealand. We currently do not know how this variant protects from T2D, but we do know that the pancreas produces a hormone called insulin, and insulin is responsible for lower blood sugar levels after a meal. When T2D develops, the pancreas's ability to produce insulin is reduced, causing a rise in blood sugar levels. In this project we will investigate whether the genetic variant in the CREBRF gene may be protecting the pancreas cells from damage, and this leads to a reduce T2D risk in some people of Māori and Pacific ancestry.

FUNDED BY: Marion Ross Memorial Fund

MEMBRANE DISRUPTION BY CYTOTOXIN AN-58 ($43,526 – 1 year) 1119016

A/Prof Christopher Squire, Dist. Prof Dame Margaret Brimble, A/Prof Adam Patterson, Dr Jeff Smaill, Dr Paul Young, Dr Iman Kavianinia, Dr Iain Hay

School of Biological Sciences,
The University of Auckland

From left to right: Distinguished Prof Dame Margaret Brimble, Dr. Iain Hay, A/Prof Christopher Squire, Dr Paul Young, Dr Iman Kavianinia, Johanes Kevin Kasim

Antibody drug conjugates (ADC) are an exciting development in treating breast cancer. These elegant engineered molecules can be envisioned as "heat-seeking missiles" that seek out cancer cells using a precision antibody and then deploy a "payload", a toxic molecule that will destroy the cancer cell. This approach towards targeted cancer therapy is exemplified by trastuzumab emtansine (tradename Kadcyla™) that can effectively treat drug resistant breast cancers. There are over 60 ADCs in development, but each of them deploys only one of two different types of cancer-killing payloads – this lack of diversity is a serious impediment to progress. To address this problem, studies led by Distinguished Professor Dame Margaret Brimble have discovered a novel cancer-killing payload called AN-58. AN-58 appears to kill cancer cells by disrupting membranes – the biological barriers that enclose and separate parts of cells. It is critical that we fully understand this cancer killing mechanism. We believe that AN-58 kills cancer cells by "punching" holes in their membranes – but seeing is believing. We will make artificial membranes that mimic cells and then use super-powerful electron microscopes to directly visualise how AN-58 destroys cancer cells.

FUNDED BY: Hugh Green Fund

ATP SIGNALLING AND COCHLEAR SYNAPTOPATHY ($108,968 – 2 years) 1119014

Dr Haruna Suzuki-Kerr, Prof Peter Thorne, A/Prof Srdjan Vlajkovic, Dr Shelly Lin

Dept. of Physiology,
The University of Auckland

A/Prof Srdjan Vlajkovic, Dr Haruna Suzuki-Kerr and Prof Peter Thorne

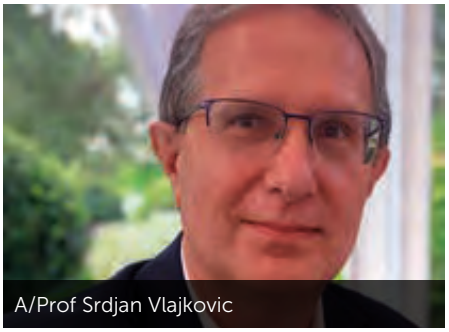
Hearing loss is a global problem; according to the 2017's report from the National Foundation of Deaf, in New Zealand, 880,000 people are estimated to be living with some degree of hearing loss in 2016. Hearing aids and cochlear implant technologies can provide improvement, albeit at significant cost to our economy, and these technologies cannot reverse the underlying pathology. There is a strong need for new therapeutic interventions to prevent the progression of underlying pathology and to facilitate recovery of the residual hearing. Our sense of hearing starts in the inner ear organ called cochlea, where "hair cells" respond to incoming sound and this information is propagated to our brain by auditory neurons. Recent research suggested the loss of communication between hair cells and neurons to be the major underlying cause of hearing loss. We have hypothesis that a group of ATP-receptor proteins are important for maintaining the connections between hair cells and neurons. In this proposal, we will test this hypothesis, in hope to identify these proteins as novel therapeutic targets that can prevent the loss of synaptic connections in the cochlea, and even reverse it by facilitating re-connection between hair cells and auditory neurons.

CO-FUNDED BY: Eisdell Moore Centre

CISPLATIN-INDUCED COCHLEAR INFLAMMATION ($159,234 – 2 years) 1119017

A/Prof Srdjan Vlajkovic, Prof Paul Smith, Prof Peter Thorne

Dept. of Physiology,
The University of Auckland



A/Prof Srdjan Vlajkovic

Cisplatin chemotherapy is considered a mainstay of cancer treatment. However, the growing population of cancer survivors demands better management of long-term side effects of cisplatin treatment. Following cisplatin chemotherapy, 40-80% of adult patients and at least 50% of paediatric patients are left with permanent hearing loss. Currently, there are no treatments available to mitigate or reverse cisplatin-induced hearing loss, other than dose reduction or switching to non-cisplatin treatments. Both alternatives may have negative impacts on cancer treatment outcomes, hence hearing loss risk must be carefully weighed against therapeutic efficacy. This pre-clinical study is focused on damaging effects of cochlear inflammation as a result of systemic cisplatin administration. We aim to investigate the molecular mechanisms that contribute to resolution of cochlear inflammation and then develop a novel strategy for preventing hearing loss associated with cisplatin chemotherapy. Proposed studies are directly relevant for the prevention of hearing loss in cancer patients treated with cisplatin and other platinum-based chemotherapeutic agents.

Grants Awarded continued

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

In this study we will use our combined expertise in clinical cardiology, cardiac electrophysiology and neurophysiology to perform novel research into the interactions between sympathetic neurons and heart cells in inherited arrhythmia syndromes. Specifically, we will focus on Long QT Syndrome (LQTS), the most common cause of sudden death in New Zealand youth. LQTS arrhythmias are typically triggered by the sympathetic "fight-or-flight" response. Treatment strategies including beta-blockers and sympathectomy (the surgical cutting of a sympathetic nerve to break the neuron-heart cell connection), although the underlying mechanisms remain poorly understood. Also, exactly how these sympathetic neurons cause cardiac arrhythmia in LQTS is unknown. Recent breakthroughs make it possible to model neuro-cardiac interactions in vitro. Using induced pluripotent stem cells (iPS cells) that we have reprogrammed from LQTS patient and control blood, we will grow sympathetic neurons and heart cells together. These co-cultures will enable us to directly study the neuronal regulation of heart rate and action potential duration using cellular electrophysiology techniques, and find out what differs in the LQTS patient-derived cells that causes the arrhythmia. A better understanding of the underlying neurocardiac arrhythmia mechanisms could enable improved risk management, tailored therapies and new treatment targets for LQTS families.

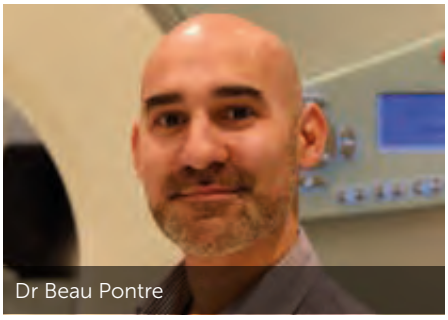
FUNDED BY: Bruce Cole Fund

GAVIN AND ANN KELLAWAY MEDICAL RESEARCH FELLOWSHIP

$44,360 1719003

Dr Beau Pontre

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



Dr Beau Pontre

To develop an Auckland-based research programme in MRI-guided radiotherapy planning through overseas experience and collaboration.

SIR HARCOURT CAUGHEY AWARD

$13,983 1719004

Prof Frank Bloomfield

Liggins Institute, The University of Auckland

Prof Frank Bloomfield

One of the most comprehensive health challenges facing New Zealand is childhood overweight. The Liggins Institute, University of Auckland, together with Uppsala University is about to implement a new strategy to prevent childhood obesity called the ECHO zone - after the World Health Oganisation report "Ending ChildHood Obesity" in which NZ played a leading role. In ECHO zones changes in society are made so that the children's immediate environment is adapted to make healthy choices. This requires long-term involvement of several stakeholders implementing the changes together. Through ongoing collection of data on how the children's health is affected by changes in environmental factors around the children, an ECHO zone builds scientific evidence for which societal changes that effectively and permanently reduce the risk of obesity and obesity. Professor Peter Bergsten is a leading exponent of the ECHO zone concept and will work with the Liggins Institute and the local community to develop an ECHO zone in Rotorua.

KELLIHER CHARITABLE TRUST EMERGING RESEARCHER START-UP AWARDS

$30,000 1719001

Dr Sarah Stewart

Department of Medicine,
The University of Auckland

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

$30,000 1719002

Dr Jia-Yun Tsai

Department of Molecular Medicine & Pathology, The University of Auckland

Research support for her Postdoctoral Fellowship 'A novel peptide delivery platform for the development of mucosal vaccines'

BOTH GRANTS FUNDED BY:
Kelliher Charitable Trust

Kelliher Charitable Trust

AMRF SUPPORT OF THE 2019 AUCKLAND DHB RESEARCH POSTER WEEK

$1,000 Award 6719007

Dr Doug Campbell

Anaesthesia, Auckland City Hospital, Auckland District Health Board

AMRF Best Directorate Award at the 2019 Auckland DHB Research Poster Week: Five posters presented by the team, including 'MASTERSTROKE - a pilot randomised controlled trial of the management of systolic blood pressure during endovascular thrombectomy for acute ischaemic stroke'.

Read more about Dr Campbell on Pages 10 and 21.

TRAVEL GRANTS

Dr Jesse Ashton

Dept. of Physiology,
The University of Auckland

To attend the Heart Rhythm Society (HRS) 40th Scientific Sessions, San Francisco, USA, 8 - 11 May 2019.

Dr Ghader Bashiri

School of Biological Sciences,
The University of Auckland

To attend the Gordon Research Conference on 'Enzymes, Coenzymes and Metabolic Pathways', Waterview Valley, New Hampshire, USA, 20 - 26 July 2019.

Dr Elizabeth Berryman

General Medicine, Waitemata District Health Board

To attend the International Conference of Digital Health, Houston, USA, 24 - 25 April 2019.

Dr Cherie Blenkiron

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

To attend the International Society for Extracellular Vesicles (ISEV) 2019 meeting, Kyoto, Japan, 24 - 28 April 2019 and the ISBER2019 annual meeting, Shanghai, China, 7 - 10 May 2019.

Dr Robert Cartwright

Oncology - Cancer Trials New Zealand

To attend the Society for Clinical Data Management EMEA 2019 conference, Berlin, Germany, 23 - 25 October 2019.

Dr Erin Cawston

Brain Research New Zealand

Laboratory visits to Prof Henrik Zetterberg, Gottenburg, Sweden and Prof Charlotte Teunissen, Amsterdam, The Netherlands, 18 October - 5 November 2019.

A/Prof James Fisher

Dept. of Physiology,
The University of Auckland

To attend the Experimental Biology 2019 conference, Orlando, USA, 6 - 9 April, 2019.

Dr Peter Freestone

Dept. of Physiology,
The University of Auckland

To attend the Society for Neuroscience annual conference, Chicago, USA, 16 - 23 October 2019.

A/Prof Michael Hay

Auckland Cancer Society Research Centre, The University of Auckland

To attend (as a keynote speaker) the 16th International Congress of Radiation Research, Manchester, UK, 24 - 29 August 2019.

A/Prof Sarah Hetrick

Dept. of Psychological Medicine,
The University of Auckland

To attend the International Society of Suicide Prevention International 30th World Congress, Derry, Northern Ireland, 17 - 21 September 2019.

Dr Joanna James

Dept. of Obstetrics & Gynaecology,
The University of Auckland

Visit to Oxford and Cambridge, UK & Vienna, Austria, to meet with collaborators, examine a rare collection of specimens, and attend the ESHRE meeting, 14 - 28 June 2019.

Dr Hannah Kersten

School of Optometry & Vision Science,
The University of Auckland

To attend the Association for Research in Vision and Ophthalmology (ARVO) annual meeting, Vancouver, Canada, 28 April - 2 May 2019.

Dr Annette Lasham

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

To attend the International p53/p63/p73 Isoforms Workshop, Dubrovnik, Croatia, 31 October - 8 November 2019.

Dr Amy McCaughey-Chapman

Dept. of Pharmacology & Clinical Pharmacology, The University of Auckland

To attend the joint ASSCR-AGCTS-ISCT scientific meeting, Brisbane, Australia, 13 - 15 November 2019.

Dr David Musson

Dept. of Medicine,
The University of Auckland

To attend (as an invited speaker) the Tissue Engineering and TERMIS EU 2019 meeting, Rhodes, Greece, 27 - 31 May 2019, and to visit a potential collaborator, Basel, Switzerland, 2 - 3 June 2019.

Dr Julia Robertson

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

To attend the Microbiology Society Annual Conference, Belfast, UK, 7 - 12 April 2019.

Dr Augusto Simoes-Barbosa

School of Biological Sciences,
The University of Auckland

To attend (as invited speaker) The Great Wall Symposium 2019, Paris, France, 23-29 September 2019.

Dr Simon Swift

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

To attend the International Society for Extracellular Vesicles (ISEV) 2019 meeting, Kyoto, Japan, 24 - 28 April 2019.

Prof Mark Vickers

Liggins Institute, The University of Auckland

To attend the 11th World Congress on the Developmental Origins of Health and Disease (DOHaD), Melbourne, Australia, 20 - 23 October 2019.

IMPROVED DIAGNOSIS OF SKIN CANCER

Dr Hannah Holtkamp

Edith C. Coan Postdoctoral Research Fellowship

Dr Hannah Holtkamp works in the Dept. of Chemical Sciences at The University of Auckland and talks about the difference the Edith C. Coan Research Fellowship will make in her life.

My research interests are identifying the current problems and challenges faced by the medical community, particularly with relevance to New Zealand, and using my skills and resources from an analytical chemistry background to come up with innovative solutions that can revolutionise how medicine is practised.

By putting together a team of experts with a broad skill set covering multiple areas of science and medicine, I have created a comprehensive project with broad benefits for science and medicine, particularly in New Zealand.

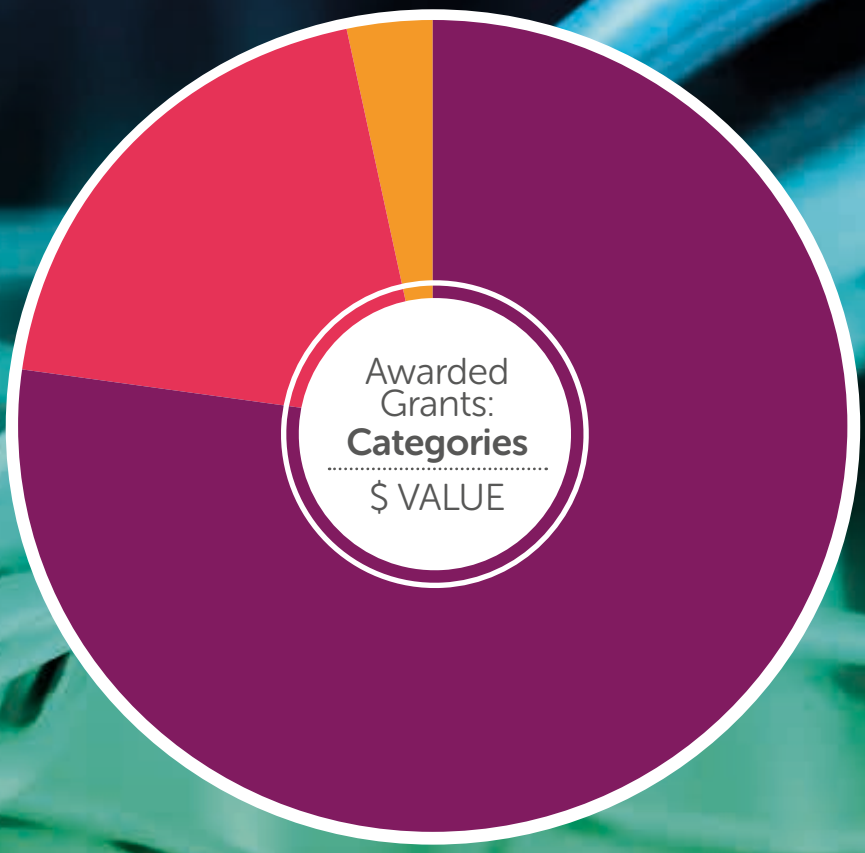
My work will contribute to a fundamental understanding of how Discoid lupus erythematosus (DLE), a largely unstudied disease with high relevance to New Zealand, differs from other skin diseases and skin cancers. It will enhance the diagnostic resolution and sensitivity needed for its detection using our newly developed Raman spectroscopy diagnostic devices. The success of these devices can create a fundamental change in the current medical approach of disease diagnosis both in New Zealand and around the world.

Disease diagnosis and photonic sensors are a burgeoning area with enormous future potential. Establishing myself in this research area will allow me to contribute to fundamental science in an academic environment, while also contributing to the production of novel medical devices used by doctors both within New Zealand and globally.

"The AMRF postdoctoral fellowship has given me the freedom to pursue my passions in science."

Read more on page 6.

GRANTS COMPLETED



2019 AWARDED GRANTS – CATEGORIES
55 GRANTS AWARDED TOTALLING $3,376,920

Biomedical	(38)	**$2,609,377**	77.3%
Clinical	(13)	**$661,299**	19.6%
Population Health and Community	(4)	**$106,244**	3.1%

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

Grants Completed

PROJECTS

EPISTASIS IN CVID ($67,415 – 1 year) 2115002

A/Prof Rohan Ameratunga, A/Prof Klaus Lehnert, Dr Euphemia Leung, Dr See-Tarn Woon

Virology and Immunology, Auckland District Health Board

From left to right: A/Prof Klaus Lehnert, Dr See-Tarn Woon, A/Prof Rohan Ameratunga, Dr Euphemia Leung

We have been fortunate to prove the existence of quantitative epistasis in humans. Epistasis is the synergistic interaction of two genetic loci leading to severe disease. We identified an Auckland family with mutations of the TACI and TCF3 genes that are involved in antibody production. We showed the most severely affected member carrying both mutations was much more severely affected than other individuals carrying only one mutation. Although the existence of epistasis was predicted over a century ago, it has been controversial because of the lack of well-characterised examples.

FUNDED BY: A. C. Horton Estate

SECONDARY LYMPHOEDEMA ($159,994 - 2 years) 1116012

Dr Jonathan Astin

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

From left to right: Janet Reid (BBiomedSc Hon candidate), Denver Britto (Phd candidate), Jonathan Astin (Group leader), Wenxuan Chen (Research Technician), Annie Yang (MSc BiomedSc Candidate)

Lymphatic vessel dysfunction causes lymphoedema - the painful, debilitating and incurable build-up of lymph in the body. In New Zealand, around 20% of women who undergo axillary lymph node removal and/or radiotherapy as part of treatment for breast cancer will develop secondary lymphoedema due to the incomplete repair of lymphatic vessels. Currently, there is very little known about how lymphatic vessels regenerate following injury, therefore with the support of AMRF, we have developed a model of lymphatic vessel repair using zebrafish, a well-established model of vascular development. Our work has shown that wound-associated macrophages are required for effective lymphatic repair – the first time these cells have been implicated in lymphatic regeneration. In addition we have uncovered a novel pathway involved in lymphatic regeneration, identifying a mutant that regenerates lymphatics 30% faster than normal. We are currently investigating the mechanism by which wound-associated macrophages and our mutant are able to enhance lymphatic vessel repair. This research is part of our longer-term aim to identify molecules and signalling pathways that can aid lymphatic repair and therefore prevent the development of secondary lymphoedema in cancer patients.

IMPROVING STENTING OUTCOME ($153,456 - 2 years) 1117003

Dr Susann Beier, Prof John Ormiston, Prof Alistair Young, A/Prof Mark Webster, A/Prof Brett Cowan

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

Dr Susann Beier

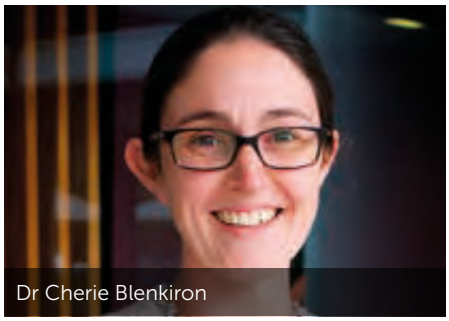
Throughout the project we successfully expanded the CTCA data collection and improved their pre-processing by using advanced segmentation methods and implementing automated processes. This led to a novel framework which we aim to publish soon, including a vessel shape analytics tool with population statistics capability. Similarly, the computational blood flow modelling has been automated and improved, which enabled us to identify 1) population groups through patient classification, 2) adverse vessel shape markers and associated bio-metric factors with 3) disease probability maps for individuals and population groups. We 3D printed selected population group representative models and are in the process of bench-top stenting these for subsequent micro-CT image analysis and two stent technique assessment. The required methods and tools have been successfully developed and piloted. To conclude, we experienced a six-month delay in progress due to relocation and personal hardship of a medical collaborator. However, we are confident to complete the remaining two tasks soon by which time all set objectives will have been successfully met. The findings and results have been published and presented in a range of leading medical and biomedical engineering platforms, and we expect further publications to arise from this work.

FUNDED BY: Bruce Cole Fund

IMMUNOONCOLOGY OF MERKEL CELL CARCINOMAS ($25,000 – 6 months) 1118005

Dr Cherie Blenkiron, Dr Kate Parker

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



Dr Cherie Blenkiron

Merkel Cell Carcinoma (MCC) is a rare but often deadly skin cancer that appears as a quickly growing painless red lump commonly on sun exposed skin. Patient trials overseas have found that half of people with MCC that has spread or metastasised respond well to immunotherapies like the Melanoma treatment Keytruda. These immunotherapies block proteins that the cancer uses as camouflage from our own attacking and protective immune system. There are many ways that a cancer can hide from the immune system - our study aimed to investigate what methods MCC may be using. With funding from the AMRF we were able to access a new technology, only available overseas to analyse some of these new proteins. This method, called Digital Spatial Profiling showed us that there are many camouflage proteins present within each patients' cancer. It also pinpointed possible new targets for trials of up and coming immunotherapies. Together this information could tailor new treatments to improve the lives of people diagnosed with MCC worldwide.

FUNDED BY: J. I. Sutherland Fund

PERIOPERATIVE ATRIAL FIBRILLATION AND POSTOPERATIVE STROKE (PAFS) STUDY ($30,743 - 2 years) 2116003

Dr Doug Campbell, Dr Tom Burrows, Dr Cornelius Kruger, A/Prof Timothy Short

Dept. of Anaesthesia, Auckland District Health Board

Dr Doug Campbell

The main NeuroVISION study has been published by the Lancet. The incidence of covert stroke was 7% and was associated with increased risk of delirium, overt stroke and cognitive decline. The PAFS substudy recruited 30 patients in New Zealand and a total of 140 patients internationally. Study follow up is now completed and further analysis will start shortly. The results may shed light on the aetiology of covert stroke and suggest therapies to prevent covert stroke.

FUNDED BY: A. C. Horton Estate

IN VIVO TARGETS OF PLACENTAL EXTRACELLULAR VESICLES ($158,372 - 2 years) 1116022

Prof Larry Chamley, Dr Scott Graham

Dept. of Obstetrics & Gynaecology, The University of Auckland

Song Paek and Prof Larry Chamley in the lab

Since the fetus is related to dad, the mother's immune system should see the placenta/fetus as a transplant and reject it. The fetus uses an elaborate system of signals that we do not yet fully understand, to prevent the maternal immune system from rejecting it. Placental extracellular vesicles are newly discovered signals that the fetus uses to communicate with its mother. It is widely believed that these vesicles may be responsible for preventing the maternal immune system attacking the fetus. While there is strong evidence this happens in test tubes, we previously found evidence that placental vesicles may not do this in pregnant animals. We have demonstrated that while placental extracellular vesicles are removed from the maternal blood within 24 hours, surprisingly there is almost no interaction between the vesicles and immune cells in the maternal blood. However, a small population of specialised cells in the maternal spleen (an immune organ) does appear to interact with a subpopulation of placental vesicles, microvesicles. Further work is required to determine if this specific interaction is important in modifying the maternal immune system during pregnancy.

Grants Completed continued

PREVALENCE OF ORAL HPV INFECTION ($151,243 – 2 years) 1115005

Dr Carol Chelimo, A/Prof Merilyn Hibma, Prof Suzanne Garland, Prof Thomas Lumley

Dept. of Obstetrics & Gynaecology,
The University of Auckland

Dr Carol Chelimo

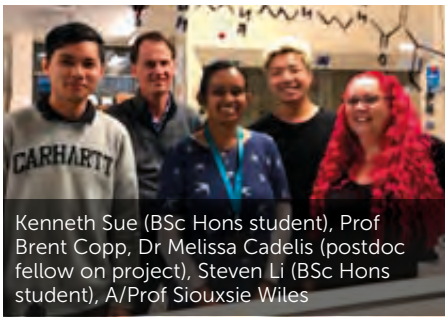
This research was undertaken to estimate the rate of oral HPV (human papillomavirus) infection in people aged 18-64 years who live in the Auckland Region. It also aimed to find out if there are difference in oral HPV rates between males and females, whether rates are lower in females who have had the HPV vaccine, and which factors make it more likely for someone to have an oral HPV infection. A total of 374 people participated in this project of whom 41% (152/374) were male and 59% (221/374) were female. By ethnicity, 23% (86/374) were Māori, 9% (35/374) were Pacific Peoples and 67% (251/374) were non-Māori non-Pacific. By age, the proportion of participants in the age groups 18-24 years, 25-34 years, 35-44 years, 45-54 years and 55-64 years were respectively 8%, 16%, 25%, 24% and 27%. Of the 370 participants who gave consent to be contacted to provide an oral sample, we were able to reach and collect samples from 270 participants (73%). The samples are currently undergoing HPV testing at a laboratory in Australia. Thereafter, the analysis to address the research aims will be completed and these findings will be shared with participants, the AMRF, and the public.

FUNDING CONTRIBUTION BY: Anonymous Donor and Pauline Gapper Charitable Trust

OVERCOMING DRUG-RESISTANT BACTERIA ($154,847 - 2 years) 1116001

A/Prof Brent Copp, Prof Jean Michel Brunel, Dr Siouxsie Wiles

School of Chemical Sciences,
The University of Auckland



Kenneth Sue (BSc Hons student), Prof Brent Copp, Dr Melissa Cadelis (postdoc fellow on project), Steven Li (BSc Hons student), A/Prof Siouxsie Wiles

Drug-resistant Gram-negative bacteria represent a global health threat to humanity. These bacteria are exceptionally difficult to treat, as the organisms possess intrinsic resistance mechanisms that make them insensitive to many antibiotics. Among Gram-negative bacteria, Pseudomonas aeruginosa is a common hospital acquired pathogen, being the second most common cause of hospital acquired pneumonia, urinary tract infection and surgical site infection. An attractive strategy for overcoming bacterial resistance is to identify compounds that can enhance the activity of antibiotics that are currently ineffective. Such drug 'rehabilitation' could help halt the spread of antibiotic resistance. Starting from a molecule related to a natural product, this two-year multi-disciplinary project led to the synthesis of a large number of new analogues that resulted in the discovery of an improved, novel compound that potentiates the action of multiple antibiotics towards multiple species of difficult to treat Gram-negative bacteria. The compound is selective in its action in that on its own it did not inhibit the growth of bacteria, nor was it toxic to cells and had no effect on red blood cells. We are currently taking this exciting discovery and exploring its potential to act as a topical additive to prevent microbial infection of burns wounds.

FIBROSIS OF THE TRANSVERSE TUBULAR SYSTEM IN HUMAN HEART FAILURE ($156,863 – 2 years) 1115014

Dr David Crossman, Prof Peter Ruygrok, Mr Maximilian Pinkham, Dr Mia Jullig, Dr Christian Soeller, Dr Carolyn Barrett

Dept. of Physiology,
The University of Auckland

Dr David Crossman

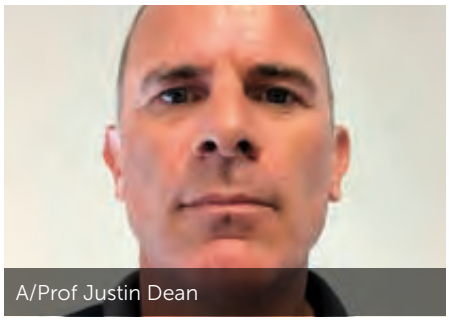
In this research, we sort to characterise the role of collagen fibrosis in the pathological remodelling of the transverse (t) tubules. T-tubules are invaginations of the plasma membrane that are responsible for electrical activation of contraction within the heart. In heart failure disruption of normal t-tubule structure leads to impaired contractility. However, it is still an open question to what drives this remodelling. In this work, we were able to document the accumulation of collagen, or fibrosis, within the t-tubules in both human and an animal model of heart failure. This research formed the basis of a project application to the Health Research Council of New Zealand that was funded in 2018. We are now further testing our hypothesis that fibrosis drives t-tubule remodelling including testing a new anti-fibrotic drug.

FUNDING CONTRIBUTION BY:
T. M. Hosking Charitable Fund

IGF-1 AND PRETERM BRAIN INJURY ($158,997 - 2 years) 1116008

Dr Justin Dean, Prof Alistair Gunn

Dept. of Physiology,
The University of Auckland



A/Prof Justin Dean

The overall aim of our study was to test whether postnatal infection in preterm infants causes deficits in insulin-like growth factor (IGF-1) signalling in the brain, and that restoring IGF-1 signalling can promote normal brain development in these infants. Using a newborn rodent model in postnatal inflammation, we found persisting deficits in brain IGF-1 signalling, which were associated with deficits in oligodendrocyte and neuronal maturation, and neurobehavioral outcomes. Further, we found that peripheral treatment with human recombinant IGF-1, or the small peptide cGP, could restore brain IGF-1 signalling and promote normal behavioural outcomes. These findings provide novel preclinical evidence that therapies based on normalizing brain IGF-1 signalling may be useful for restore normal brain development after preterm infection/ inflammation.

FUNDING CONTRIBUTION BY:
N. R. Thompson Trust

perpetual guardian

CALCIUM SCORES AND MICRORNAS ($47,112 – 2 years) 1115017

Dr Nikki Earle, Prof Vicky Cameron, Prof Rob Doughty, Dr Anna Pilbrow, A/ Prof Malcolm Legget

Dept. of Medicine,
The University of Auckland

Dr Nikki Earle

This study aimed to identify new biomarkers for early stage heart disease, allowing us to target people at high risk with preventative interventions such as medications or lifestyle modifications before symptoms occur. We measured a range of different research biomarkers to see if they are associated with coronary artery disease at an early stage where plaques build up in the arteries. These are being measured in blood samples from people who have had the amount of plaque in their arteries estimated using specialised imaging techniques. Recruitment of the 192 participants is complete with clinical data collected and blood samples obtained. Laboratory analysis of collected samples is underway for six different research biomarkers with results from this study to be available in early 2020.

FUNDED BY: Bruce Cole Fund

WHANAU EXPERIENCE OF A HEALTHY HOMES INITIATIVE ($14,259 - 1 year) 1118001

Dr Kyle Eggleton

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

Dr Kyle Eggleton

This study has looked at the health benefits gained from undertaking healthy homes initiatives. Two forms of initiatives were explored. The first initiative involved providing insulation, furnishings and blankets to whānau and the second initiative looked at more significant remedial work, such as plumbing, electrical work and roofing required to make a home more habitable. 20 whānau have been interviewed for the study, the majority of whom were Māori. The findings from the study are that although physical health benefits can occur there are also non-physical health benefits. This study demonstrated that healthy homes initiatives can create a sense of 'place' in which participants felt that their home was more 'home like'. As a result non-physical health benefits became apparent such as improved social cohesion and mental wellbeing, children becoming more child-like and family peacefulness and contentment from 'homeliness'. The implications for practice are that healthy homes initiatives should consider the role of 'place' in creating a healthy home environment. Wider health benefits may accrue through assisting people to create a home-like environment.

Grants Completed continued

PROGNOSTIC MODEL FOR BREAST CANCER ($68,223 – 1 year) 1117011

Prof Mark Elwood, Dr Sandar Tin Tin, A/Prof Vernon Harvey, A/Prof Roger Marshall, A/Prof Ian Campbell

Dept. of Epidemiology and Biostatistics,
The University of Auckland

Dr Essa Tawfiq, Prof Mark Elwood and Dr Sandar Tin Tin

For a woman diagnosed with breast cancer, her long-term outcome depends on a large number of factors. Having a reasonable estimate is important to the woman personally and for the consideration of treatment options. To look beyond the major indicators such as stage of disease, doctors in New Zealand sometimes use 'predictive models'. These are complicated statistical models which look at the effects of many factors and combine them to estimate long-term outcome. With AMRF funding, we developed a predictive model based on the experience of New Zealand patients diagnosed in Auckland and in the Waikato over the last 15 years. We have shown that the accuracy of the predictions is very good, compared to the actual experience of these women. This complex work needed a team that included epidemiologists and surgeons, and was only possible because women with breast cancer have contributed their data to specialised clinical registries. The next question we want to answer is whether the New Zealand prediction, applied to our patients, is as good or possibly superior to the UK system. We are planning to work with colleagues in University of Cambridge in England to compare the UK and NZ systems.

FUNDED BY: Hugh Green Fund

EXPLOITING BRAIN MECHANISMS TO PROTECT FROM PRETERM BRAIN INJURY? ($159,263 - 2 years) 1117009

A/Prof Mhoyra Fraser

Dept. of Physiology,
The University of Auckland

A/Prof Mhoyra Fraser

Previously, we have shown that following an acute severe episode of asphyxia (oxygen deprivation) to the preterm fetal sheep brain, treatment with the Toll-like receptor 7 agonist, Gardiquimod (GDQ), which activates immune responses, conferred neuroprotection to the developing white matter cells, 3 days following injury. This was associated with induction of immunosuppressive type cells within the white matter of the fetal brain and increased circulating levels of anti-inflammatory cytokine proteins (IFN-β and interleukin-10; Scientific reports 9, 9562). However, brain injury can continue to evolve even after secondary cell death has subsided. Thus, our present studies sought to determine whether GDQ was neuroprotective after 7 days recovery from asphyxia. Results showed that GDQ administration was associated with significantly increased levels of the anti-inflammatory cytokine, IL-10, within the fetal circulation during the first 48 hours after asphyxia. Despite this immunomodulatory response, there were no significant differences found in the number of white matter cells. In conclusion, the results suggest an inability to demonstrate significant neuroprotective properties for the white matter cells most likely relates to the lack of long-term efficacy of GDQ and that further experiments are required using a longer treatment regimen.

REGULATION OF DOPAMINE RELEASE BY ENDOCANNABINOIDS ($150,019 - 2 years)

1116016

Dr Peter Freestone, Prof Janusz Lipski

Dept. of Physiology,
The University of Auckland

Dr Peter Freestone

The chemical transmitter dopamine underlies many of our basic behaviours, including movement. However, the exact mechanism determining the timing and magnitude of dopamine release in the brain remain unknown, limiting our ability to effectively treat diseases in which dopamine release is affected, such as Parkinson's disease. A key brain region called the subthalamic nucleus could control or modulate the activity of dopamine-producing neurons possibly via a mechanism using endocannabinoids – cannabis-like substances produced naturally in the brain. This project used advanced electrochemical techniques to precisely measure – more than previously possible – the exact level of dopamine in the rat brain. We found a new subdivision in the pathway between the subthalamic nucleus, dopamine neurons and a new target for dopamine release in the 'tail' of the striatum. Dopamine release was smaller and longer lasting than in the conventional dopamine pathways, possibly underlying a unique function of this new pathway in movement behaviour. While it remains to be seen if endocannabinoids are involved, the new pathway offers an exciting avenue of further study to better understand how dopamine is released in the normal brain, and potential new therapies to rectify abnormal dopamine release.

Read more inside the back cover.

CB1 IN BRAIN CANCER ($157,272 - 2 years) 1116011

A/Prof Michelle Glass, Dr Scott Graham, Dr Graeme Finlay

Dept. of Pharmacology & Clinical Pharmacology, The University of Auckland

A/Prof Michelle Glass

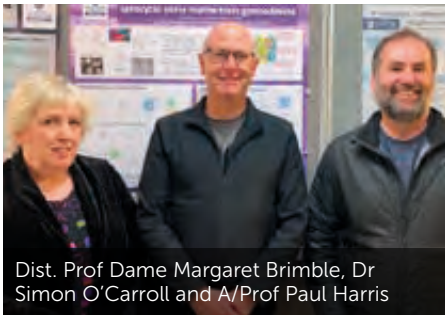
Cannabis has suggested to be a treatment (or even a cure) for brain cancer, yet there is very limited data on this. In this study we used brain cells grown from human tumours (collected by the Auckland Cancer Society Research Centre) to examine if brain tumour cells express functional cannabinoid receptors, and if so, whether activating them lead to cell death. Interestingly, our study found that almost half of the tumour cells did express a functional cannabinoid CB1 receptor. However, although these receptors signalled at relevant concentrations of cannabinoids, cell death only occurred at very high concentrations - and occurred whether there were cannabinoid receptors present or not. More concerning, even "normal" non cancer cells died at these concentrations of cannabinoids. Thus our study does not currently support the suggestion that cannabinoids could positively impact on brain cancer progression.

FUNDING CONTRIBUTION BY:
Pauline Gapper Charitable Trust

LIPOPEPTIDES TO TREAT NEUROLOGICAL DISEASE ($158,507– 2 years) 1117016

A/Prof Paul Harris, Dr Simon O'Carroll, Dr Sung Yan, Dist. Prof Margaret Brimble

School of Biological Sciences, The University of Auckland



Dist. Prof Dame Margaret Brimble, Dr Simon O'Carroll and A/Prof Paul Harris

In conditions such as spinal cord injury (SCI), tissue damage can spread and is caused by transfer of neurotoxins from the damage site to otherwise healthy tissue via intercellular channels called connexin hemichannels. We can 'block' these channels at the time of injury, using small protein molecules called peptides, to reduce the damage. However, these molecules are not very stable in the body. In this project we modified this peptide in order to make it more stable and therefore a more promising candidate to treat conditions such as SCI.

DEVELOPMENT OF A THYMIDYLATE SYNTHASE BIOMARKER ($138,702 - 2 years) 1116023

A/Prof Nuala Helsby, Dr Frederik Pruijn, Dr Matthew Strother, Prof Michael Findlay

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

Dr Katie Burns, A/Prof Nuala Helsby, Alice Cho, Dr SooHee Yeong and Umaiyaall Shanmugaraajah

Thymidylate synthase (TS) is one of the important targets of the anticancer drug 5-FU. Inherited differences in this enzyme have been reported to influence treatment outcomes. These associations often rely on measuring the amount of immunoreactive protein in tumour tissue. Our aim was to develop a biomarker for this enzyme (known as the F-dUMP-TS complex). Low levels of TS activity and F-dUMP-TS biomarker formation was detectable in cells. However, we found that numerous TS-related proteins were detectable in different types of cells. This complicates the previous assumptions about a direct relationship between inherited genotype and protein expression. One of these modifications (phosphorylation of the protein) had identical electrophoretic behaviour to the F-dUMP-TS complex. This is likely to limit the use of the F-dUMP-TS complex as a discriminatory biomarker of response to 5-FU treatment. We also found that the standard method for genotyping samples was not optimal and are continuing to assess other ways of analysing this highly repetitive region of the genome. Ultimately, our investigations may help us to find more appropriate ways to measure the expression of functional thymidylate synthase enzyme in patient samples. This could also help determine whether inherited differences in the thymidylate synthase gene do or do not influence response to 5-FU treatment in cancer patients.

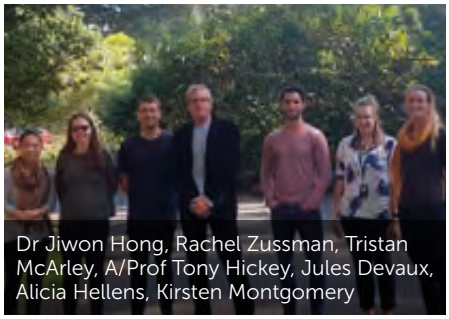
FUNDED BY: Anonymous Donor

Grants Completed continued

NEW MEDIATORS OF ACUTE DISEASE ($159,663 – 2 years) 1115007

Dr Anthony Hickey, Dr Anthony Phillips, A/Prof Adam Patterson, Dr Jiwon Hong

School of Biological Sciences,
The University of Auckland



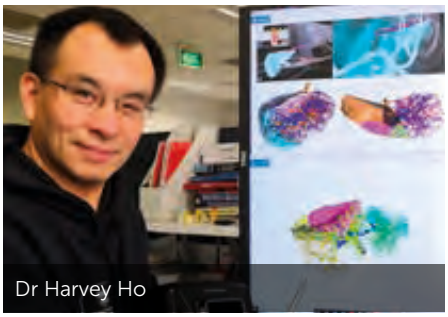
Dr Jiwon Hong, Rachel Zussman, Tristan McArley, A/Prof Tony Hickey, Jules Devaux, Alicia Hellens, Kirsten Montgomery

A range of conditions (sepsis, heavy blood loss, inflammation) can cause acute disease that results in similar patterns of multiple organ failure (heart and lungs, then kidneys and liver) and suggests common disease factor or factors. Gut derived lipid particles are transported in the lymph and are altered in a rat model of sepsis. We proposed these particles may carry toxic components to the key organs, and promote organ failure by damaging mitochondria. Here we studied lymph from different disease models we aimed to: 1) Isolate triglyceride-rich lipoproteins from the intestinal lymph of 5 rodent models (sepsis, haemorrhagic shock, acute pancreatitis, intestinal ischemia/reperfusion injury, sham). 2) Then perform compositional analyses (proteins, metabolites, lipids, small non-coding RNAs) of triglyceride-rich lipoproteins, and 3) determine if triglyceride-rich lipoproteins can change the cellular function of rodent primary heart and lung cells. 4) We further explored whether diseased triglyceride-rich lipoproteins can change the mitochondrial function of rodent primary heart and lung cells and analyse the oxidative damage capability of acute disease-conditioned triglyceride-rich lipoproteins. Differences in lymph-derived lipids were found and these suppressed mitochondrial function in lung and heart tissues.

AUGMENT REALITY AIDED LIVER ABLATION ($110,139 - 2 years) 1116020

Dr Harvey Ho, Dr Peter Swan, Dr Adam Bartlett, A/Prof Andrew Holden

Auckland Bioengineering Institute,
The University of Auckland



Dr Harvey Ho

Minimally invasive tumour ablation is a rapidly growing technique in treating liver cancer patients. In this project we have used Virtual Reality and Augmented Reality (VR/AR) technologies to develop pre-surgical planning and intra-operational navigation tools to assist liver ablation. We used inexpensive VR devices and a custom-designed ablation probe rig for fast prototyping of VR/AR systems. Different versions of the system can be either adapted to different use scenarios, run from a desktop computer with VR gadgets or operated from a mobile device such as a mobile phone or a tablet. In addition, we have developed the key algorithms including the liver segment simulation for liver-specific applications. The algorithm is to address the problem that liver segments are invisible from the liver surface but such a segmental anatomy needs to be followed in liver surgery. This cutting-edge algorithm is highly costly if purchased from abroad. We have also developed a statistical liver shape model that can be used to quantitatively describe the geometric variations in most healthy and diseased livers. The financial support from the AMRF grant has helped us to publish two journal papers and four peer-reviewed conference papers during the project timeframe.

FUNDED BY: W. & W. A. R. Fraser Charitable Trust

SILDENAFIL TREATMENT OF GROWTH RESTRICTION AND GLUCOSE METABOLISM ($33,538 – 18 months) 1117004

Dr Anne Jaquiery, Ms Hui Hui Phua, Ms Emma Buckels, Dr Charlotte Oyston

Liggins Institute, The University of Auckland

Dr Charlotte Oyston, Dr Emma Buckels, Eric Thorstensen, Prof Frank Bloomfield, Dr Anne Jaquiery, Hannah Maxwell

Fetal growth restriction (FGR) is associated with increased fetal morbidity and increased risk of developing metabolic disease later in life. There is currently no proven effective clinical treatment for FGR. Maternal sildenafil citrate treatment has been shown to improve fetal growth in FGR lambs. However, it has not been determined whether this treatment also mitigates the adverse metabolic effects of FGR. We aimed to identify, in sheep, the mechanisms by which placental insufficiency–induced FGR affects gene and protein expression in metabolically active tissues, and whether sildenafil treatment ameliorates these adverse expression patterns. We explored the expression of key markers of glucose metabolism in fetal pancreas and muscle. Our findings suggest that, in males, maternal sildenafil treatment may mitigate negative effects of FGR on insulin-mediated glucose transport and metabolism in skeletal muscle; whereas in females, sildenafil treatment may mitigate the negative effects of FGR on insulin synthesis in the pancreas. Further, the greatest effect of sildenafil treatment in the pancreas was on glucagon-secreting alpha cells, rather than insulin-secreting beta cells. We are further exploring this novel finding. Sildenafil is already being used to treat pregnant women with FGR, so it is important to understand the mechanisms underlying the observed outcomes.

UNDERSTANDING THE CREBRF VARIANT ($159,266 - 2 years) 1117006

Dr Troy Merry, Prof Peter Shepherd, Dr Rinki Murphy, A/Prof Lindsay Plank

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

From left to right: Betty Shih (research assistant), Dr Troy Merry (PI), Hannah Burden (PhD student)

The aim of this project was to investigate how a variant in the CREBRF gene increases body mass index (BMI) but protects from type 2 diabetes. This variant is almost exclusively found in people of Polynesian ancestry. We have now measured the body composition (via DXA scan) of >250 males of Māori or Pacific descent who are aged 20-45 years with BMI<40. Of this, >60 participants have the CREBRF variant, and on average they have more lean mass (muscle) and the same proportion of fat mass as those without the CREBRF variant. This strongly suggest the CREBRF variant is not a fat-mass related variant as originally hypothesised. Having greater lean mass may provide a reason to why the CREBRF variant is protecting from type 2 diabetes. Therefore, we undertook detailed analysis of how people with the CREBRF variant metabolise sugar. Unexpectedly, we found that CREBRF variant is not better able to metabolise sugar but may have increased ability for their pancreas to produce the hormone insulin. This is important because a reduced ability for the pancreas to produce insulin is associated with the development of type 2 diabetes.

BARIATRIC SURGERY AND THE GUT MICROBIOME ($96,743 - 2 years) 1116015

A/Prof Rinki Murphy, Ms Naomi Davies, A/Prof Justin O'Sullivan, A/Prof Lindsay Plank

Dept. of Medicine,
The University of Auckland

A/Prof Rinki Murphy

We compared hormonal, body composition and gut bacteria changes in obese people with type 2 diabetes (T2D) following randomisation to either Roux-en-Y gastric bypass or sleeve gastrectomy bariatric surgeries. We identified similar increases in insulin, GLP-1 and GIP gut hormones following both types of surgeries at 1 year. Diabetes remission (mean 74%) and weight loss (mean 30kg) were similar for both groups, with 80% of weight loss being accounted for by fat mass loss alone. We observed a 9% decrease in muscle mass following surgery, similar for both surgery groups. Bone density loss following RYGB and SG was minor – 5% and 3% respectively, although all started with high bone mass. Participants in the RYGB group felt less hungry (p=0.01) and had less desire to eat (p=0.03) 1 year after surgery, compared to those in the SG group. Using fecal samples collected before and 1 year after surgery, we identified several bacterial taxa present in the baseline gut in those who went on to remit from T2D following surgery, independent of surgery type. Further work to explore their role as novel probiotics or biomarkers of diabetes remission is indicated.

HORMONAL MARKERS OF DIABETES AFTER ACUTE PANCREATITIS ($108,702 - 2 years)

1116021

Dr Max Petrov, Dr Rinki Murphy

Dept. of Surgery,
The University of Auckland

A/Prof Max Petrov (front row, second from left) with research group

The project aimed to investigate the pancreatic hormone and gut hormone responses to mixed meal test in individuals with new-onset prediabetes or diabetes after acute pancreatitis. We found that decreased insulin sensitivity, β-cell compensation, and no significant change in secretion of glucagon and pancreatic polypeptide characterise these participants. They are also characterised by increased levels of gastric inhibitory peptide and decreased levels of oxyntomodulin. The above findings may help develop an evidence-based protocol with a view to optimising control of glucose homeostasis in new onset prediabetes or diabetes after acute pancreatitis.

FUNDING CONTRIBUTION BY:
Marion Ross Memorial Fund

Grants Completed continued

EPIGENETICS OF PROGESTERONE RESISTANCE IN ENDOMETRIOSIS ($157,141 - 2 years)

1116005

Dr Anna Ponnampalam, Prof Cynthia Farquhar

Liggins Institute, The University of Auckland

Dr Anna Ponnampalam presenting research poster

The project is to test the hypothesis that DNA methylation/hydroxymethylation plays a crucial role in the aberrant estrogen priming of the endometrium that lead to progesterone resistance and development of endometriosis. We have so far determined the hormonal regulation of the enzymes responsible for DNA hydroxymethylation in endometrium. We are currently in the process of finalising the experiments and analysing the results to determine the role of DNA hydroxymethylation in estrogen signalling and progesterone resistance in the endometrium. This grant has not only given us financial assistance to perform the highlighted research but also allowed us to establish valuable collaborations with other researchers in Australia as well as communicate with consumer groups who are servicing women suffering from endometriosis. I want to take this opportunity to thank the AMRF and sponsors for the valuable work they do.

MUCOSAL VACCINATION AGAINST S. AUREUS WITH PILVAX ($100,650 - 2 years) 1116007

Dr Fiona Radcliff, A/Prof Thomas Proft

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

Dr Fiona Radcliff (in red) with the Pilvax team

The aim of this project was to test whether PilVax - a novel platform for delivery of mucosal vaccines - could confer protective immunity from infection with live bacteria. Selected vaccine candidate antigens from Staphylococcus aureus, a significant human bacterial pathogen, were successfully inserted into PilVax. Vaccination stimulated strong antibody responses to the introduced S. aureus antigen in the nose and lungs of mice. These animals were then exposed to live S. aureus using a non-invasive model of mucosal infection. Unexpectedly, mice immunised with PilVax or PilVax with S. aureus peptide had significantly reduced levels of infection compared with unvaccinated controls. This is an important observation as eliminating S. aureus infection in the mucosa is a challenging but clinically important problem. S. aureus positive patients are more likely to contract a serious infection after major surgery, therefore it is common to premptively treat with local antibiotics and antiseptics to minimise this risk. Vaccination or alternative strategies for stimulating immune cells offer the promise of a more targeted approach. Future studies in this area will aim to understand how this effect is mediated and also to assess the suitability of PilVax for delivering more complex vaccine antigens from S. aureus.

FUNDED BY: John and Poppy Stilson Endowment Trust

perpetual guardian

KNOWLEDGE-BASED RADIOTHERAPY TREATMENT PLANNING ($134,391 – 2 years)

1115021

Dr Andrea Raith, Prof Paul Rouse, Prof Matthias Ehrgott, Dr Juliane Manitz, Dr John Simpson, Dr Giuseppe Sasso, Dr Andrew Macann

Dept. of Engineering Science, The University of Auckland

Dr Andrea Raith, Dr Peppe Sasso and Dr Andrew Macann

Radiotherapy treatment is used to treat cancer in about 50% of all NZ cases. During treatment a patient's tumour volume is irradiated while avoiding damage to surrounding healthy tissue. Treatment plans are developed by a planner using commercial software in an often time-consuming iterative process, which aims to achieve a range of plan quality parameters. The oncologist reviews the plan and decides to go ahead, or that re-planning is required (which may or may not lead to actual improvement of a plan). It is impossible to tell if a plan is truly optimal; plan acceptance and quality are based on experience and intuition. We developed a knowledge-based benchmarking approach to assess plan quality by on-the-fly comparison of a new plan to a library consisting of previous clinically approved plans. Integrating this approach in current planning systems gives planners and oncologists feedback on plan quality avoiding unnecessary iterations, thus improving the efficiency of the planning process. A machine-learning based approach that can ultimately help individualise treatment goals to patients was also developed. Patients can benefit from receiving better quality treatments as the developed approach indicates improvement potential for the planner to focus on.

PERIOPERATIVE VASCULAR EVENTS IN UNRECOGNISED OBSTRUCTIVE SLEEP APNOEA ($157,880 – 2 years) 2114014

A/Prof Timothy Short, Dr Ivan Bergman, Dr Joyce Tai, Dr Maartje Tulip

Dept of Anaesthesia & Perioperative Medicine, Auckland City Hospital

Dr Timothy Short

Unrecognised obstructive sleep apnoea increases cardiovascular risks in the general population, but whether obstructive sleep apnoea poses a similar risk in the perioperative period when respiration is also depressed by respiratory depressant drugs such as opioids for pain relief and the residual effects of anaesthesia remains uncertain. In this study we performed preoperative screening and testing for obstructive sleep apnoea in adults with cardiovascular risks having major surgery who did not have a prior diagnosis of obstructive sleep apnea. Those adults who were found to have severe obstructive sleep apnoea were found to have a markedly increased risk of cardiovascular complications including heart attack and death. We plan to confirm this finding in a further study of these patients and to investigate whether high flow nasal oxygen can improve breathing and oxygenation of patients and decrease the incidence of these complications of surgery.

CYSTEINE PHARMACOKINETICS AND DOSE RESPONSE ($130,256 – 2 years) 1115011

A/Prof Malcolm Tingle, A/Prof Janie Sheridan, Dr David Newcombe, Dr Natalie Walker

School of Pharmacy,
The University of Auckland

A/Prof Malcolm Tingle, Soo Hee Jeong, Prof Janie Sheridan and Rhys Ponton

The aim of this study was to explore how the clearance of a drug cytisine from the body is effected by dose and how often the dose is given and how this may impact on safety and tolerability.

The study was able to show that the drug was safe and well tolerated at all doses studied and that drug concentrations were entirely predictable by computer modelling based on our previous data.

Unfortunately we were unable to complete the second study due to prolonged delays getting a new supply of the drug from the manufacturers and the fact that a different pharmaceutical company has applied our studies to design a larger clinical trial for registration purposes, rendering the continuation of the final study of limited applicability.

THE PROGNOSTIC SIGNIFICANCE OF IMMUNE CELL INFILTRATES IN MENINGIOMA ($10,432 - 2 years) 2116013

Dr Clinton Turner, Prof Mike Dragunow, Prof Maurice Curtis

Anatomical Pathology, Auckland District Health Board

Dr Clinton Turner

Meningiomas are tumours of the covering layer (the dura) of the central nervous system. This project aimed to examine whether the composition of the immune reaction in the tumour influenced the risk of tumour recurrence. This has entailed examining the immune cell infiltrate in 508 meningiomas removed from 465 people over a 10 year period with various immune cell markers. Detailed computer assisted image analysis has been performed on around 10,000 individual tissue sections from these tumours. The laboratory work has been completed and detailed statistical analysis is currently being performed with final results expected midway through next year. In addition, data from the study population is being analysed to provide local incidence and recurrence rates for meningioma within the Auckland region.

POSTDOCTORAL FELLOWSHIPS

EDITH C. COAN RESEARCH FELLOWSHIP

ENDOSCOPIC MAPPING OF GASTRIC SLOW WAVES ($199,473 & $30,000 - 2 years)

1316001 & 1717002

Dr Timothy Angeli

Auckland Bioengineering Institute, The University of Auckland

Dr Tim Angeli in the Target Laboratory

My AMRF Edith C. Coan Fellowship aimed to develop and validate a minimally-invasive endoscopic diagnostic device to detect the abnormal electrical patterns occurring in the stomachs of patients with severe gastrointestinal disorders, to provide a quicker, more efficient, and more cost-effective diagnosis. The Fellowship was highly successful. A prototype endoscopic mapping device was developed, and the safety and efficacy of the device were validated in pre-clinical trials. Analytical algorithms for interpolating, visualising, and quantifying the slow wave data were developed and validated, creating a computational pipeline for analysing endoscopic recordings. The effects of gastric distension, electrode size, and electrode material were defined in pre-clinical trials to validate the current prototype design and inform future refinements to the device. Ethical and District Health Board (DHB) approvals were secured, a comprehensive protocol for tracking, maintaining, and reprocessing of the devices was developed and approved by DHB administration, and clinical trials are underway. During the fellowship, I authored/co-authored 11 journal papers, 2 journal editorials, 2 conference proceedings, and 15 conference abstracts. I have also recently been awarded a Rutherford Discovery Fellowship from the Royal Society of New Zealand, enabling me to continue this research for the next 5 years.

FUNDED BY: Edith C. Coan Trust & Kelliher Charitable Trust

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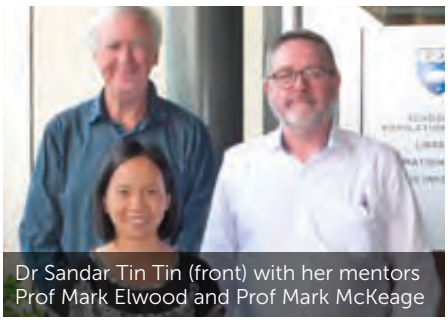
THE DAVID AND CASSIE ANDERSON RESEARCH FELLOWSHIP

GENE MUTATION, GENETIC TESTING AND TARGETED THERAPY IN LUNG CANCER ($193,377 & $30,000 – 2 years)

1315002 & 1716002

Dr Sandar Tin Tin

Section of Epidemiology and Biostatistics, The University of Auckland



Dr Sandar Tin Tin (front) with her mentors Prof Mark Elwood and Prof Mark McKeage

This research aimed to better understand genetically-defined forms of lung cancer, and the impact and uptake of genetic testing and targeted therapy in the New Zealand patient population. The data from the New Zealand Cancer Registry, pharmacological information database, TestSafe, laboratory records and medical records were extracted through the three waves of data collection. The findings showed that the uptake of genetic testing was suboptimal in New Zealand, particularly among Māori patients. A considerable number of untested patients could harbour a mutation, thereby missing an opportunity to be treated with targeted therapy. To date, three peer-reviewed journal articles have been published and the findings have also been presented in a number of national and international conferences. The fellowship has helped me expand my knowledge, skills and experiences in cancer epidemiology, strengthen collaboration with colleagues from other disciplines and develop my research career in the field of cancer. It has also provided me with an opportunity to supervise three student research projects (one summer student, one masters and one doctoral project).

FUNDED BY: David and Cassie Anderson Medical Trust & Kelliher Charitable Trust

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NAMED FELLOWSHIPS

DOUGLAS GOODFELLOW REPATRIATION FELLOWSHIP

DEVELOPING ZEBRAFISH ETV6 MODELS OF ACUTE MYELOID LEUKEMIA (AML) FOR CHEMICAL SUPPRESSOR SCREENS ($376,437 – 2 years with an extension of $195,924 – 1 year) 1413001 & 1413001-1

Dr Andrew Wood

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

Dr Andrew Wood

Acute Myeloid Leukaemia (AML) is an aggressive blood cancer where abnormal "myeloid" white blood cells multiply and crowd out the healthy blood cells leading to death. AML is treated with high dose chemotherapy, and often bone marrow transplant. Despite intensive therapy, many patients do not survive. Unfortunately, progress in improving AML therapy and outcomes has been frustratingly slow.

The two main chemotherapy drugs used to treat AML fifty years ago are still the main drugs used today. The lack of progress owes to many factors, but part of the challenge is the relative paucity of AML models that can be studied in the lab. To help overcome these limitations we developed a new model to explore the biology of AML. We used a small transparent tropical fish with stripes called a zebrafish, but surprisingly enough zebrafish blood is very similar to human blood. We engineered the zebrafish blood stem cells to express gene mutations that cause AML in people. This makes some of the zebrafish develop an excess of myeloid white blood cells that makes the fish sick. We hope this model will provide new biological insights into AML, and ultimately lead to better therapies.

FUNDED BY: William Douglas Goodfellow Charitable Trust

RUTH SPENCER MEDICAL RESEARCH FELLOWSHIP

ANTERIOR RESECTION SYNDROME: A PATHOPHYSIOLOGICAL DEFINITION ($282,500 – 2 years) 1415003

Dr Celia Keane

Dept. of Surgery,
The University of Auckland

Dr Celia Keane (right) with Supervisor Prof Ian Bissett and Kirsty Wing, the NZ patient representative for the international LARS consensus definition group

The broad aim of this project was to advance the understanding of Low Anterior Resection Syndrome (LARS), which is the term used to describe bowel dysfunction after resection of rectal cancer. This work showed that there is huge variation in the way that this bowel dysfunction is reported (and measured) and led to the formation of an international patient-provider collaboration which developed a consensus definition of LARS. The prevalence of LARS was found to be 71% and various risk factors associated with the development of LARS were identified from an analysis of patients undergoing this surgery in Auckland and Dunedin Hospitals. Strategies such as avoidance of or early closure of ileostomy, or re-infusion of ileostomy output using a novel device, have been investigated as potential ways to mitigate the dysfunction these patients experience after resection.

FUNDED BY: The Ruth Spencer Estate

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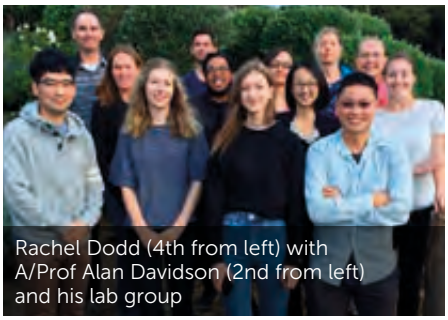
DOCTORAL SCHOLARSHIPS

BARBARA BASHAM DOCTORAL SCHOLARSHIP

HUMAN GENETIC STUDIES OF FAMILIAL KIDNEY DISEASE ($126,500 – 3 years) 1214003

Miss Rachel Dodd

Dept of Molecular Medicine & Pathology,
The University of Auckland



Rachel Dodd (4th from left) with A/Prof Alan Davidson (2nd from left) and his lab group

The aim of this project was to study a candidate mutation in a New Zealand family with a genetic health condition that includes effects on the kidney (FSGS) and reproductive system (bicornuate uterus, hypospadias). Through next-generation sequencing of patient DNA, the mutation suspected to be responsible was identified in an important functional domain of the Wilms' Tumour 1 (WT1) gene. This domain helps regulate the expression of a network of downstream target genes in the urogenital systems. Our approach was to create kidney organoids (mini kidneys in a dish) and compare the effects of the mutation on this system, and our results showed that mutant WT1 has reduced ability to activate a number of these downstream target genes. There are already a number of known WT1 mutations associated with similar syndromes, however this specific case represents a previously unidentified WT1 mutation with a novel set of symptoms. This work adds to the existing body of knowledge regarding genetic causes of FSGS, and WT1-associated syndromes. It has also given us the tools to test potential therapeutic compounds in further work using this system. It is hoped that this work will ultimately lead to improvements in treatment and screening.

FUNDED BY: Barbara Basham Medical Charitable Trust

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BRIAN DE LUEN DOCTORAL SCHOLARSHIP

UNDERSTANDING GABA SIGNALLING IN HUMAN PERICYTES IN HEALTHY AND ALZHEIMER'S DISEASE BRAINS ($111,500 & $30,000 - 2 years, 5 months) 1216002 & 1717003

Mr Karan Govindpani

Dept. of Anatomy and Medical Imaging,
University of Auckland

Karan Govindpani with his doctoral supervisor Dr. Andrea Kwakowsky

GABA is a key neurotransmitter in the human brain. It functions by binding to GABA receptors (GABARs) on the surface of cells, precipitating changes in cell function. There have been suggestions that GABA acts directly on brain blood vessels and plays a role in the control of blood flow and other vascular functions. In this study, we sought to examine how GABA exerts this effect in the human brain, as the control of brain blood flow has important implications for cerebral health and for diseases like Alzheimer's disease (AD). We

demonstrated the expression of GABARs on blood vessels in healthy post-mortem human brain tissue and showed that the receptor subunit composition changes in AD blood vessels. Vessels are composed of cell types including pericytes and endothelial cells. We showed a unique GABAR subunit expression in cultures of these cells at the RNA and protein level and proved that pericytes and endothelial cells do not contain intracellular GABA stores. Thus, we were able to prove the existence of a novel type of GABAR in human brain blood vessels, but it remains to be seen what function it holds in health and disease and several studies are ongoing to answer this question.

FUNDED BY: Brian De Luen Estate & Kelliher Charitable Trust

Kelliher Charitable Trust

RISK FACTORS, PATHOPHYSIOLOGY AND MANAGEMENT OF DIVERTICULAR DISEASE ($126,500 – 3 years) 1214005

Dr Rebekah Jaung

Dept. of Surgery,
The University of Auckland

From left to right: Dr Rebekah Jaung, Dr Tony Milne, Dr Celia Keane, Dr Anthony Lin

There are over 2000 acute hospital admissions for diverticular disease (DD) across New Zealand annually. This doctorate aimed to increase our understanding of the disease process behind DD and improve clinical management of acute diverticulitis (AD). 1) We have recruited the largest prospectively collected acute diverticulitis dataset in the country. This data will be used to formulate a scoring system to assess severity in AD and predict need for operative intervention and increased patient support. This is intended to be a tool to help prioritise imaging and operations, especially for clinicians practising in hospitals with limited resources. 2) We have used high resolution manometry (HRM) to measure large bowel motility in twelve participants with colonic diverticulosis. These readings have been compared to those of control participants and the results are currently being prepared for publication. This is the first HRM study of diverticulosis and will increase our knowledge of the role of motility in DD. 3) We have completed the first placebo-controlled randomised control trial of antibiotics versus placebo in uncomplicated AD. The results of this trial have been submitted to an academic journal for publication, and will add to the evidence base around the best practice treatment of AD.

GAVIN AND ANN KELLAWAY MEDICAL RESEARCH FELLOWSHIP

$37,556 1518002

Prof Edwin Mitchell

Dept. of Paediatrics: Child and Youth Health, The University of Auckland

The specific aim of this application for the Gavin and Ann Kellaway Medical Research Fellowship was for me to spend time in Seattle working with the Microsoft data scientists and Seattle Children's Hospital learning about these new analytical research tools, and how they can be applied to "Big Data" here in New Zealand to identify new risk factors and insights for Sudden Unexpected Death in Infancy (SUDI).

$34,895 1517001

Prof Boyd Swinburn

School of Population Health,
The University of Auckland

The Global Syndemic of obesity, undernutrition and climate change was defined by the Lancet Commission on Obesity as the paramount health challenge of the 21st century. This radial idea of combining these three seemingly separate, intractable pandemics into a single concept represented a completely different way of seeing these global challenges as being highly inter-connected with potentially common solutions called double or triple-duty actions. The Gavin and Ann Kellaway Medical Research Fellowship allowed me to test and refine these ideas ahead of publication of the report in Lancet in January 2019. I presented the ideas in eight workshops (236 expert attendees) in the US (two workshops, including to the World Bank), UK, Vienna (to many UN agencies), Tehran, Buenos Aires (to attendees at a satellite meeting to the International Congress on Nutrition), Delhi, and Wuhan. The feedback greatly improved the robustness and the narrative for the Lancet Commission on Obesity report. Substantial media activity has followed publication of the report and many subsequent presentations around the world.

SIR HARCOURT CAUGHEY AWARD

$14,127 1718001

Prof Cynthia Farquhar

Dept. of Obstetrics & Gynaecology,
The University of Auckland

This grant was used to fund travel for Professor Johannes Evers, of Maastricht University in the Netherlands, and Editor in Chief of Human Reproduction, to attend the Core Outcome Measures for Infertility Trials (COMMIT) meeting in Auckland from the 27 to 30 November 2018. Fifteen healthcare professionals, six researchers, and nine people with infertility, representing 27 countries, participated in the consensus development meeting. A manuscript is currently being prepared for publication.

SUMMIT POSTDOCTORAL RESEARCH PRESENTATION AWARD

$3,000 Travel Award 6718001

Dr Marie-Claire Smith

Dept. of Medicine,
The University of Auckland

In June 2018 I was honoured to receive the AMRF prize for best oral presentation at a conference for post-doctoral researchers

at the University of Auckland Faculty of Medical and Health Sciences. This prize funded my travel to Japan in 2019 to present my work to a lab group at the Tokyo Metropolitan Institute of Science and at a large international conference in Kobe. My work is on predicting recovery of the hand, arm and walking after stroke. We have developed two algorithms (decision trees) which can help a clinician or scientist predict how much movement a person is likely to recover in their hand and arm by 3 months after stroke, and how long it is likely to take for them to be able to walk by themselves again. This information is important to help patients, their families and their clinical teams to make plans for their recovery and for adjusting to life after stroke. I would like to thank the AMRF for the generous funding for this travel. Without the support of AMRF I would not have been able to travel to Japan for these talks and to share, on an international stage, some of the world-leading research that New Zealand is producing.

FUNDED BY: A.C. Horton Estate

HEALTHEX EMERGING RESEARCHER AWARD

$2,000 Travel Award 6718003

Mr Sam Blanchett

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

This award allowed me to travel to the Federation of European Microbiologists 8th congress in Glasgow, Scotland. As a major conference it draws delegates from across the world and I was able to present my PhD work to a wide audience during the poster session and engage with the global scientific community. While in the United Kingdom I also took the opportunity to visit the Francis Crick Institute. This £750 million biomedical research facility is located in the heart of London and is one of the premier research facilities in Europe. I was able to meet with an immunology group to discuss research and form a number of connections. I also attended the Society for Mucosal Immunology's conference in Brisbane where I was once again able to present my work during the poster session. This conference was a fantastic opportunity to gain insights into, and network within an exciting and dynamic field of immunology. This conference trip has been a fantastic opportunity to present my research to a global audience and I am incredibly thankful to the AMRF for the opportunity their funding helped provide.

$2,000 Travel Award 6716003

Mr Maximilian Joret

Dept. of Neurosurgery, Auckland District Health Board

Attended the European Association of Neuro-oncology, Stockholm, Sweden, 10-14 October 2018 to present his research titled 'Pericytes contribute to tumour immune system evasion in glioblastoma multiforme through the under-expression of ICAM-1, VCAM-1 and MCP-1'.

FUNDED BY: Wellington Sisters Charitable Trust

$2,000 Travel Award 6718004

Mr Luis Knight

Dept. of Physiology, The University of Auckland

Through the generous support of the AMRF, I was able to attend and present my research the 2019 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting, held in Vancouver, Canada. ARVO is a regarded as the largest and most respected eye and vision research organisation in the world with nearly 12,000 members from over 75 countries attending this conference. At this conference, I was invited to give an oral presentation of my recent PhD findings to experts in the retina field. Given that this is the most attended international eye meeting, the invitation to present is a rare opportunity for graduate students. The opportunity to present my work, gain feedback on my work, and form new networks in the retina field has been invaluable to the development of my career. It also has inspired a renewed excitement about my research and I am eager to get back into the laboratory to start experiments and get more results. This would not have been possible without support from the AMRF and I am deeply grateful to the AMRF for granting me this award and supporting my research.

$2,000 Travel Award 6717003

Miss Sarah Mitchell

Liggins Institute, The University to Auckland

Attended the Strategies and Techniques for Analyzing Microbial Population Structures (STAMPS) Workshop held annually at the Marine Biology Laboratory (MBL) of the University of Chicago, U.S.A, 29 July – 8 August 2018.

$2,000 Travel Award 6716002

Mr Hans Vellara

Dept. of Ophthalmology, The University to Auckland

Attended an international conference to present his research titled 'In vivo orbital compliance in thyroid eye disease'.

FUNDED BY: Wellington Sisters Charitable Trust

UNDERSTANDING HIGH BLOOD PRESSURE AND NEW MANAGEMENT STRATEGIES

A/Prof James Fisher
Dept. of Physiology,
The University of Auckland

A/Prof James Fisher is clear about how AMRF funding will help him and Professor Julian Paton better understand high blood pressure.

"It is a really great time to be involved with cardiovascular and respiratory physiology research in Auckland. My work is helping to bridge the gap between the work of academic and clinical scientists."

I am very grateful to the AMRF for this award. It's tremendously valuable in helping us establish an experimental facility to simultaneously monitor blood pressure, breathing, blood flow and sympathetic nerve activity – the first of its kind in New Zealand.

This funding has kick started a new collaboration between University-based physiologists and hospital-based clinicians within the new Centre of Heart Research, Manaaki Mānawa.

We're working to better understand why people have high blood pressure (hypertension), a global problem estimated to affect one billion people worldwide and one in three New Zealanders. It can cause strokes, kidney damage and heart failure, but often it goes undetected. Alarmingly, half of those patients prescribed medication for hypertension do not have their blood pressure well controlled. Why is this? Some patients are resistant to treatment and others fail to take their pills.

To address the lack of new medications, drug resistance in patients and poor compliance, future research needs to understand the mechanisms that operate to sustain high levels of blood pressure in patients.

A/Prof James Fisher

Professor Julian Paton

Our studies will investigate whether sensors within the body that detect oxygen and carbon dioxide become hyperactive and drive up blood pressure.

Our findings may help to understand a novel mechanism for why people become hypertensive. Such information will be critical for developing new management strategies to control blood pressure using both drugs and medical devices. Results already indicate great potential in two new approaches for reducing the activity of these sensors and lower blood pressure.

If you are interested in volunteering in any of our studies please contact **ana.sayegh@auckland.ac.nz** for more information.

This generous award will not only have important scientific implications, but also significant implications for my career advancement here in Auckland. I cannot emphasise enough my gratitude to Auckland Medical Research Foundation donors for their support.

Read more on page 12.

CORTICAL EXCITATION-INHIBITION BALANCE IN HEALTH AND DISEASE

Ms Rachael Sumner

Dept. of Psychology,
The University of Auckland

One third of patients diagnosed with major depressive disorder will not respond to available treatments, making depression a significant challenge for clinicians as well as patients. Hampering advancement in novel treatment development is a lack of knowledge of the neurobiological underpinning of depression. Neuroimaging methods such electroencephalography (EEG) combined with computational modelling techniques such as dynamical causal modelling have promising utility in providing accurate, useful, direct, and non-invasive in vivo measures of central nervous system disorders such as depression.

There has been a recent surge in interest in ketamine as an antidepressant as it not only works in 70% of people with treatment resistant depression, but is also an attractive tool for understanding the neurobiology of depression itself because of its rapid onset of relief from depressive symptoms. Using EEG and computational modelling this project successfully demonstrated the first evidence in humans that long-term potentiation mediated mechanisms of neural plasticity may underlie the antidepressant properties of ketamine. Ketamine was also found to alter sensory error processing. Earlier in this project, the utility of these measures were also demonstrated in the menstrual cycle. Future directions of this research include merging the two contexts to understand menstrual linked mood disorders.

($87,000 - 2 years) 1216006

FUNDING CONTRIBUTION BY:
N. H. Taylor Charitable Trust

"I would like to thank the AMRF for providing me with this scholarship and the opportunities it afforded me. In particular the travel fund allowed me to visit experts in my field. This had a major impact on the techniques I used to analyse my data and I was able to develop lasting international collaborations. Thank you to the generous donors to the AMRF, in particular to the N.H. Taylor Charitable Trust who helped to fund my scholarship."

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2019 ANNUAL RESEARCH AWARDS

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

Financial Highlights 2019

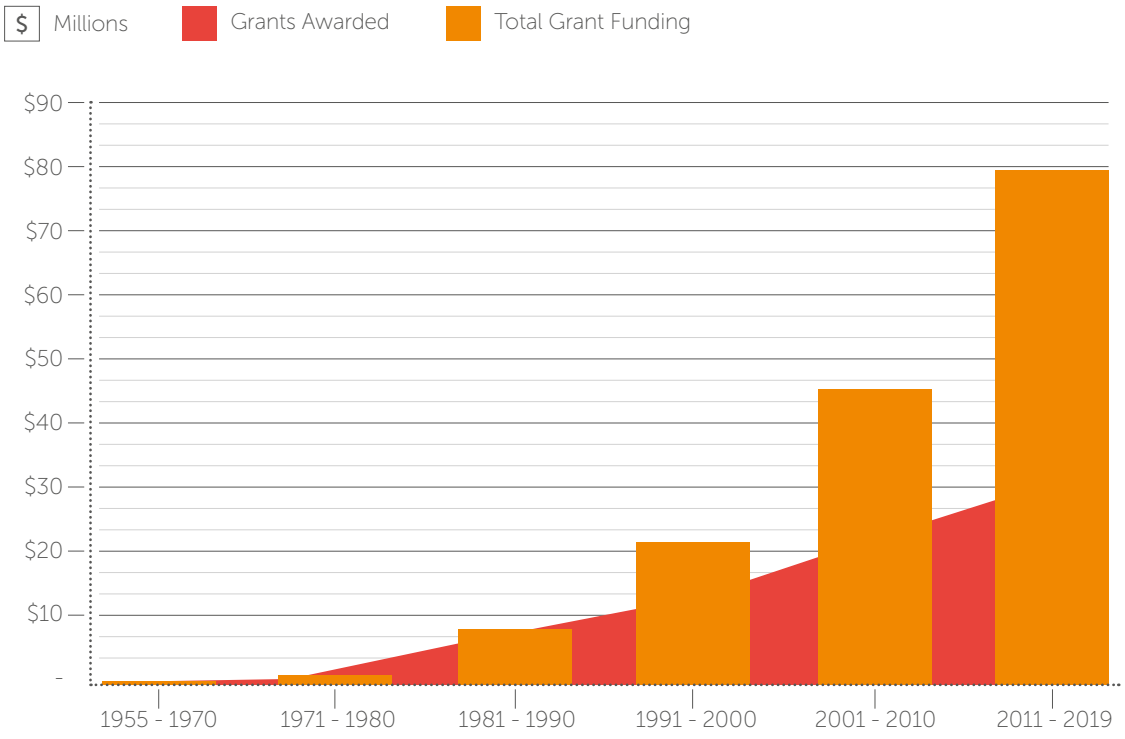
RESEARCH FUNDING 2019 $3.38 MILLION TOTAL RESEARCH FUNDING SINCE 1955 $79.3 MILLION

FINANCIAL PERFORMANCE

	Note	2019 $		2018 $	
Revenue					
Donations/Research Income	1	1,319,142		1,762,184	
Investment Income (Total Return)	2	10,980,646		20,414,388	
Other Comprehensive Revenue / (Expense)	1	301,866		1,171,968	
Total		**12,601,654**		**23,348,540**	
Expenditure					
Operational expenses		536,694		504,970	
(Less Donation)	3	(536,694)	-	(500,182)	4,788
Net Research Grant Expenditure	4		2,994,011		4,037,550
Net Surplus / (Deficit)			**9,607,643**		**19,306,202**
Trust Equity			**61,964,088**		**52,378,978**

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 - 2019



Notes to the 2019 Financial Report

1. Donation & Trust Income includes grants, donations and external funding received from the following organisations:

Perpetual Guardian Administered Funds	
Edith C. Coan Trust	180,000
Estate of Edith Rose Isaacs	100,000
John A. Jarrett Trust	40,000
C. E. Lawford Estate	3,750
Rose Richardson Estate & Trust	33,763
Room-Simmons Charitable Trust	30,000
The J. & P. Stilson Endowment Trust	100,000

Public Trust Administered Funds	
Audrey Simpson Trust	4,750
Ralph Dingle Trust	2,100
Pauline Gapper Charitable Trust	5,650
Reed Charitable Trust	12,000
Wellington Sisters Trust	5,450

Other Trusts/Funds	
Anonymous	300,000
Douglas Goodfellow Charitable Trust	132,813
The J. I. Sutherland Fund	100,000
The Kelliher Charitable Trust	60,000
Marion Ross Fund	70,670

2. Investment Income (Total Return)

During the financial year 2018 and early 2019, the Foundation restructured its investment portfolio moving from individual securities into managed funds. Investment income is now recognised and recorded on a Total Return basis, with all direct income (interest and dividends) and portfolio gains or losses (where appropriate) recorded via the Statement of Financial Performance. Whilst there are no changes to financial performance, 2018 figures have been re-classified in 2019 Financial Statements. The variance reported for the year 2019 compared to 2018 in main relates to realised gains on sale of the individual investments for the one-off transition to the managed fund portfolio during 2018.

3. Operational Expenses

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

4. Research Funding Awarded 2019

PROJECT GRANTS (19)	2,489,420
AMRF General Purpose & Named Funds Supporting Research Projects: Anonymous	
A. C. Horton Estate	
Bruce Cole Fund	
Curtis-Tonkin Fund	
Hugh Green Fund	
J. I. Sutherland Fund	
Marion Ross Memorial Fund	
MRI ERD Trust	
Paul Stevenson Memorial Trust	
POSTDOCTORAL FELLOWSHIPS (1)	200,306
AMRF Postdoctoral Fellowship	
DOCTORAL SCHOLARSHIPS (3)	274,000
AMRF Doctoral Scholarships	
AMRF TRAVEL GRANTS (19)	50,038
OTHER GRANTS	
Goodfellow Repatriation Fellowship Extension	132,813
AMRF Senior Research Fellowship	100,000
Kelliher Charitable Trust Emerging Researcher Start-up Grant (2)	60,000
Sir Harcourt Caughey Award	13,983
Gavin and Ann Kellaway Medical Research Fellowship	44,360
HealtheX Emerging Research Awards (3)	7,000
Summit Award	3,000
ADHB Award	1,000
WDHB Award (2)	1,000
TOTAL GRANT FUNDING 2019	3,376,920
Less amounts allocated but not required	(382,909)
NET GRANT EXPENDITURE 2019	**2,994,011**

Special Acknowledgements

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

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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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As a supporter of AMRF, you can help our researchers to find answers – answers that will change lives forever.

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You can choose to leave your gift of cash or assets for a specific area of research or general purposes. A sample clause to add to your will is:

"I give to the Auckland Medical Research Foundation (Charity Registration Number CC22674) [item/specific gift or value/fraction of estate residue] for its general purposes and I direct that the receipt of the Treasurer or other duly authorized officer shall be a sufficient discharge to my Executors."

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Giving a major gift during your lifetime is another way to create a lasting legacy of life – and enjoy the tax benefits.

"Gavin and I chose to do this to be able to feel the excitement of giving. I encourage those of you thinking of giving to do so in your lifetime to be able to see the research you are hoping for." Ann Kellaway.

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UPDATE FROM THE AMRF 2018 DAVIS & CARR SENIOR RESEARCH FELLOW

Dr Peter Freestone

Department of Physiology,
The University of Auckland

Parkinson's disease is a particularly cruel disorder. It impacts your movement and mobility and even the ability to interact socially.

Investigating why one section of the brain deteriorates and how to combat the condition has been a 10-year quest for emerging leader in biomedical research, Dr Peter Freestone.

Peter's pioneering the use of cutting-edge technology, called optogenetics, to improve the understanding of what happens to the brain of someone with Parkinson's.

Optogenetics is a relatively new technique in neuroscience, involving the use of light to activate single neurons within a tightly interconnected network, and allows a very high level of precision when studying brain function.

His research aims to deepen the understanding of what changes in the Parkinson's brain and identify more effective therapies to improve the lives of those living with the disease.

Peter's new collaboration with Dr Luke Hallum at the University of Auckland's Department of Mechanical Engineering, they are conducting multi-electrode array recordings from cortical brain regions, the background of this page shows individual neuron activity in vivid colour.

Read more on Page 24.

FUNDED BY: Estate of Ernest Hyam Davis & The Ted and Mollie Carr Endowment Trust

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

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