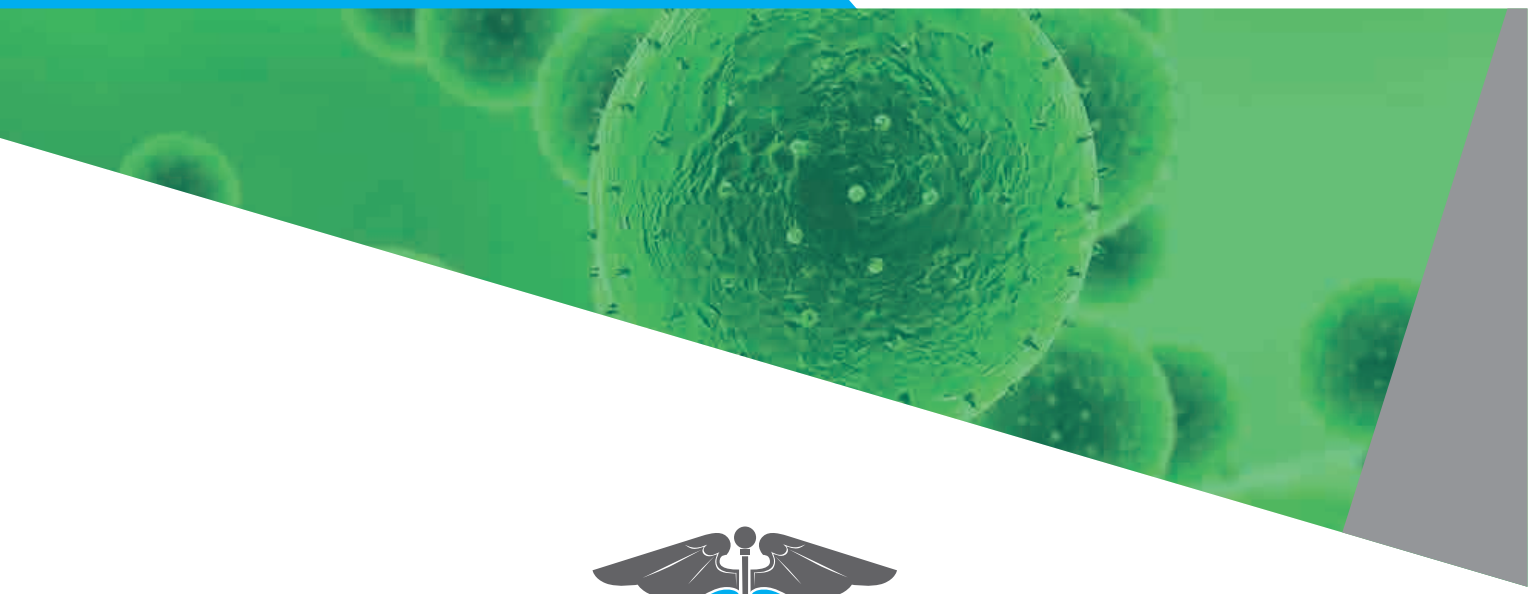

Auckland Medical Research Foundation

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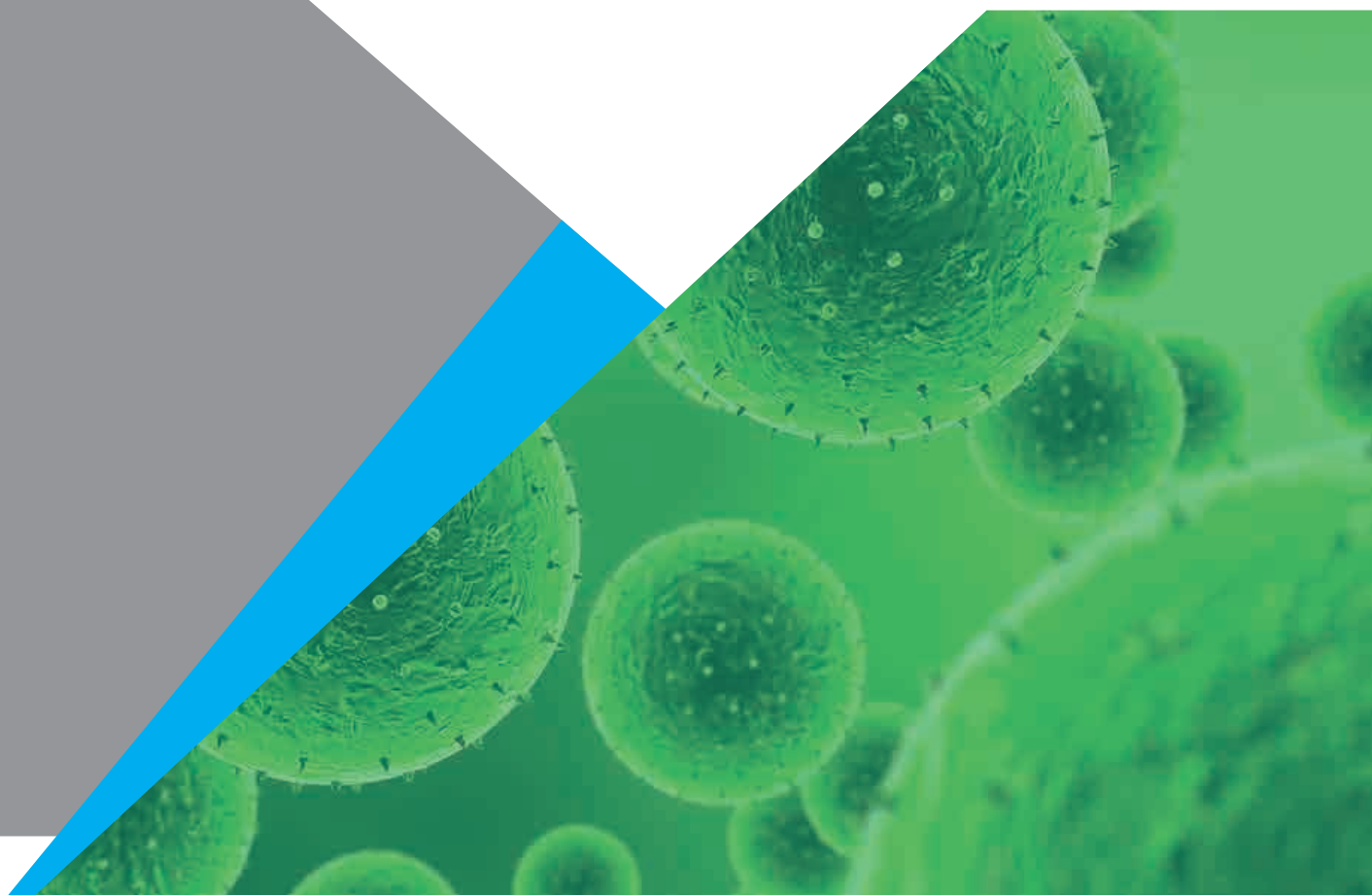
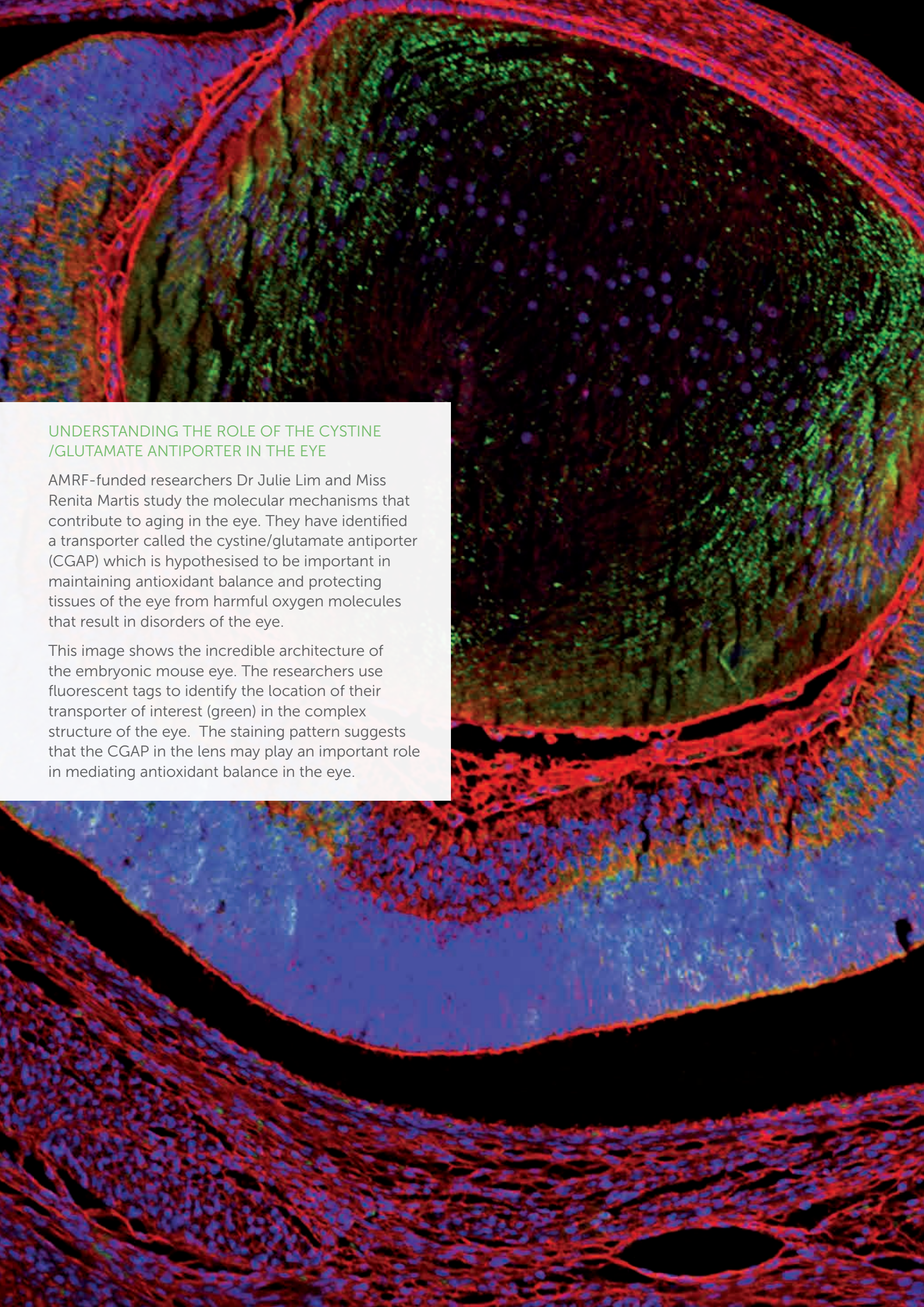
ANNUAL REPORT 2016

SUPPORTING MEDICAL RESEARCH FOR OVER *60 years*

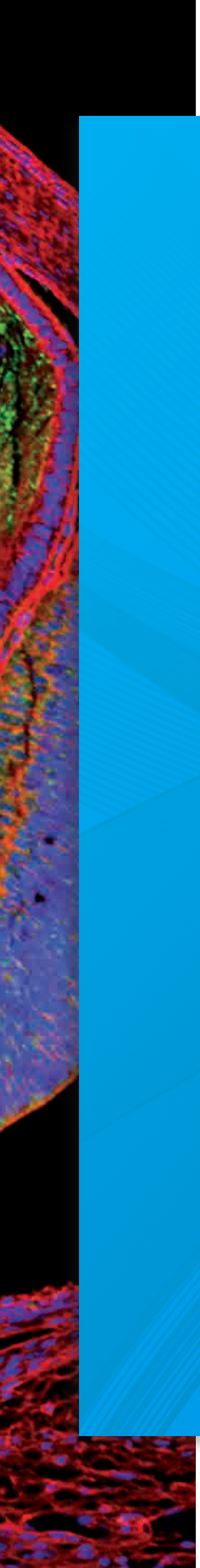




UNDERSTANDING THE ROLE OF THE CYSTINE /GLUTAMATE ANTIPORTER IN THE EYE

AMRF-funded researchers Dr Julie Lim and Miss Renita Martis study the molecular mechanisms that contribute to aging in the eye. They have identified a transporter called the cystine/glutamate antiporter (CGAP) which is hypothesised to be important in maintaining antioxidant balance and protecting tissues of the eye from harmful oxygen molecules that result in disorders of the eye.

This image shows the incredible architecture of the embryonic mouse eye. The researchers use fluorescent tags to identify the location of their transporter of interest (green) in the complex structure of the eye. The staining pattern suggests that the CGAP in the lens may play an important role in mediating antioxidant balance in the eye.



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MEDICAL COMMITTEE

Prof Peter Browett BMedSci, MBChB, FRACP, FRCPA	Chair
Dr Jane Alsweiler MBChB, FRACP, PhD	Ad hoc member (November 2016)
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A/Prof David Christie MSc, PhD	Deputy Chair (retired April 2016)
Prof Nicola Dalbeth MBChB, MD, FRACP	
Dr Justin Dean BSc Tech, MSc Tech, PhD	Ad hoc member (November 2016)
Dr Peter Fong MBBS, FRACP	
A/Prof Andrew Grey MBChB, MD, FRACP	
Dr Paul Harris BSc, MSc, PhD	Ad hoc member (November 2016)
Prof Debbie Hay BSc (Hons), PhD	October 2016
A/Prof Michael Hay BSc (Hons).PhD	From October 2016
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Dr Simon O'Carroll BSc, MSc, PhD	Ad hoc member (October 2016)
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A/Prof Ashvin Thambyah BSc (Hons), MSc, PhD	Ad hoc member (From June 2016)
Prof Peter Thorne CNZM, BSc, DipSc, PhD	
Dr Grace Wang BA (Hons), MHSc (Hons), PhD	Ad hoc member (November 2016)

STAFF

Ms Kim McWilliams	Executive Director
Mrs Kathryn Baty	Finance Manager
Dr Hannah Gibbons BSc (Hons), PhD	Research Programme Manager
Dr Jessica Costa BS, PhD	Development Manager
Mrs Ginette Clarke	Executive Assistant

REGISTERED OFFICE

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Ph: 09 923 1701
Web: www.medicalresearch.org.nz
Charity Commission Registration Number: CC22674

President's Report & Medical Committee Report

YEAR ENDED 31 DECEMBER 2016

Jeff Todd

President's Report

Now into our seventh decade, the AMRF holds to its strong belief that significant advances in medicine can come about only through well-funded, quality research. The Foundation has once again in 2016 supported these advances by awarding $3.6 million in research grants for projects, scholarships and fellowships, travelling fellowships and travel grants.

The Foundation is generously supported by an annual endowment which covers our operating expenses, meaning that every dollar donated by our loyal donors, supporters and external funding partners is used for funding the research grants that we award. We sincerely thank all donors for their valuable support.

2016 was an exciting year with highlights including our biannual public lecture series which was well attended, the publication of a new brochure "Giving Life in your Lifetime", our members only cocktail event hosted at the Kelliher Trust Gallery, and the announcement of a $2.5 million commitment to the University of Auckland's "Campaign for all Our Futures" that will provide income annually to support an AMRF Senior Research Fellow, a prestigious 5 year Fellowship targeted to future research and/or clinical leaders.

The Foundation's operations have been professionally managed by Kim McWilliams, our Executive Director and her small team of four staff. On behalf of the Board I thank them for their tireless work which ensures the Foundation runs smoothly and continues to expand its capital base while increasing research funding in a very competitive philanthropic environment.

As we go to print, I am sorry to report that, after nearly seven years' outstanding service with the Foundation, Kim has accepted another position as NZ Lead for the Private Wealth Network based in Auckland, and will be phasing out her executive role with us over the next few months. We will undertake a search for her replacement in due course. Kim has served us well and leaves the Foundation with our best wishes.

Thanks also to the trustees, board committee chairs and members who all contribute generously with their time, experience and expertise. In particular, I thank the Medical Committee, chaired by Professor Peter Browett, whose demanding but essential work in reviewing applications for grants absorbs many hours in evaluation and assessment. My special thanks to Associate Professor David Christie who after being a member of our Medical Committee for 25 years and a trustee for 9 years, has retired from both the AMRF and his position at the University of Auckland. We wish him all the best for his future.

Thanks to all of you, our stakeholders. With your loyal support and commitment, we can confidently continue seeking important advances in medicine and treatments for future generations.

Jeff Todd
President

Prof Peter Browett

Medical Committee Report

Spread between the 5 grant rounds of 2016, the Medical Committee worked voluntarily to assess 146 applications, of which 58 grants totalling over $3.6 million were successfully awarded. Particular highlights were the awarding of 4 Doctoral Scholarships, 1 Postdoctoral Fellowship and a 1 year extension to the Douglas Goodfellow Repatriation Fellowship, highlighting the AMRF's role in supporting young and emerging researchers. Although the total number of grant submissions was down this year in comparison to previous years (primarily due to changes in our eligibility criteria and our Medical Research Fellowships already being awarded in recent years) and the success rate seems high (39.7%), it still means that many worthy research projects are unable to be supported.

In 2016 we farewelled our Deputy Chair Associate Professor David Christie who had contributed more than 25 years - and an exceptional amount of knowledge - to the Medical Committee. He will be missed, but we wish him well in his retirement. I also want to extend my sincere thanks to Associate Professor Andrew Grey who provided valuable insight through his extensive knowledge of the medical research arena during the 7 years he sat on the Committee and also to Professor Cameron Grant and Dr Peter Fong for their input into the Committee over several years. This year we welcomed A/Prof Michael Hay, from the Auckland Cancer Society Research Centre, University of Auckland, to our Committee as a full member.

I would like to thank Kim McWilliams and her small team for their support of the Medical Committee throughout the year. In particular my thanks go to Dr Hannah Gibbons (Research Programme Manager) for her stewardship of the Grants portfolio, and to Leigh Harrison of ElseApps Ltd for the continued development of the AMRF portal (our fully web-based electronic application and assessment system).

Peter Browett
Chair, Medical Committee
Professor of Pathology,
Department of Molecular Medicine and Pathology,
University of Auckland

KNOWLEDGE GAINED THROUGH RESEARCH MEANS BETTER PATIENT CARE AND IMPROVED MEDICAL TREATMENTS

AMRF EXISTS FOR ONE PURPOSE: to improve the health of New Zealanders through funding the highest quality medical research. We believe that such research is vital to making genuine advances in patient care and medical treatments. But that research comes at a cost...

GROWING A SUSTAINABLE FUND

Funding for medical research in New Zealand is critical for our future health. In 1955 a group of Auckland medical and business leaders, united in their concerns about serious shortfalls in funding for medical research, came together to form the AMRF. From small beginnings, they grew a sustainable and enduring investment fund to provide research grants every year.

OUR COMMITMENT TO FUNDING EXCELLENCE

Our Medical Committee (comprised of clinical and biomedical scientists) appraises every request for funding and will consider applications from every field of modern medicine. Only the best applications meet our rigorous standards when assessing the medical and scientific importance of new research proposals.

SUPPORTING THE BEST NEW ZEALAND RESEARCH TALENT

AMRF have supported many successful scientists in New Zealand including Prof Sir Peter Gluckman, Sir Brian Barratt-Boyes and Prof Sir Graham Liggins.

Through our funding, we help to establish and retain our best emerging talent, repatriate key researchers and build capability in the New Zealand research community.

YOUR DONATION IS APPLIED ONLY TO MEDICAL RESEARCH

We apply 100% of donations, bequests, legacies and income from investments to medical research. Our operating expenses are met by a separate charitable fund. So if you donate to the AMRF, you can be assured that every cent of your donation is applied to advancing the highest quality medical research.

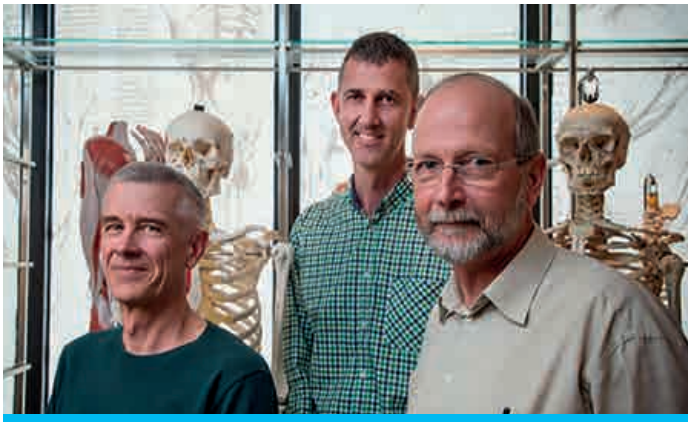
A SELECTION OF FIELDS SUPPORTED BY YOUR DONATIONS

Arthritis | Asthma | Biomedical Imaging | Bones & Muscles | Cancer | Cardiovascular | Cellular & Molecular Biology | Diabetes | Gastrointestinal | Endocrinology | Hearing | Immunology | Infectious Disease & Vaccine Development | Kidney | Liver | Lungs | Maternal & Newborn Health | Mental Health | Neuroscience & Neurological Disease | Nutrition | Pancreatitis | Population Health | Reproduction | Skin Biology & Wound Healing | Stem Cell Biology | Surgery | Vision

An AMRF Success Story

OSTEOPOROSIS AND BONE DISEASE – BIG STEPS FORWARDS

Distinguished Professor Ian Reid
(Photo courtesy of The University of Auckland)



Left to Right: Associate Professors Andrew Grey and Mark Bolland, and Distinguished Professor Ian Reid in the AMRF Medical Sciences Learning Centre. (Photo courtesy of The University of Auckland)

Since 1955, donations to AMRF have supported researchers like Distinguished Professor Ian Reid, who has developed and improved treatments for osteoporosis and bone disease in his 30+ years in research.

"AMRF has been a constant companion along the research road that we have walked and has been critically important for all the major research groups in Auckland in helping people."

"They're a vital part of the research scene in Auckland."

The Auckland Medical Research Foundation is proud to have supported the Bone and Joint Research Group for over 35 years. In 1984 Professor Ian Reid, who leads the group's clinical studies, received the first of many AMRF fellowships and grants, funded by generous donations and benefactors.

In the 1980s, Professor Reid performed the first successful trial of bisphosphonates, drugs which slow or stop the natural process that dissolves bone tissue. He addressed the novel question of whether these agents could manage osteoporosis, where bones become brittle and fragile. With initial positive responses of increased bone density in patients, he worked with pharmaceutical companies as they improved the drug formulations to be more potent, allowing for the drug to only need to be taken yearly or even once every five years. Today bisphosphonate drugs can result in a 50% reduction in fracture risk in those with osteoporosis.

In addition, Professor Reid has led the development of the use of potent bisphosphonates in Paget's disease, the debilitating bone condition that has affected up to 7% of older New Zealanders. It's a chronic, painful disorder that can result in enlarged and misshapen bones.

Prof Reid presented the Autumn 2016 AMRF Free Public Lecture to over 150 attendees in the AMRF Auditorium at the University of Auckland Medical School. His lecture discussed the impact and treatment of bone diseases, including osteoporosis and Paget's disease. As he said on the night, "Keeping bones strong over a lifetime is a longstanding challenge in medical health research and treatment."

The AMRF is grateful to the Royal Society of New Zealand for contributing to this story.

Dr David Musson operates the 'Cell Gym', a device used for the application of mechanical strain on bone and muscle cells.

OVER 30 YEARS OF AMRF SUPPORT FOR THE BONE AND JOINT RESEARCH GROUP

Distinguished Professor Ian Reid receives receives the Rutherford Medal from Minister Steven Joyce. (Photo courtesy of Royal Society of New Zealand)

Left to Right: Associate Professor Andrew Grey, Distinguished Professor Ian Reid and Associate Professor Mark Bolland with Prime Minister John Key. (Photo courtesy of Prime Minister's Science Prizes Secretariat)

RESEARCH HIGHLIGHTS

- Development of bisphosphonates for the treatment of osteoporosis, now the most widely used medicines in this area.
- Determination of the risks and benefits of calcium supplements in managing osteoporosis. They have minimal effects on bone density and fracture risk, but significantly increase the risk of heart attack, and probably stroke.
- Treatment of Paget's disease. We are now able to effectively cure this disabling bone condition in most patients who suffer from it.
- Identification of the key role that fat mass plays in determining bone density and risk of fracture. There is a myriad of biochemical connections between fat tissue and bone which mediate these relationships.
- Re-appraisal of the role of vitamin D in general health and in osteoporosis management, particularly through meta-analyses that Distinguished Professor Ian Reid has done in collaboration with Associate Professor Mark Bolland.

SUMMARY OF AMRF AWARDS

Number	Award
13	AMRF Project Grant
1	Kelliher Emerging Researcher Start-up Award
5	Scholarships and Fellowships
5	AMRF Travel Grant

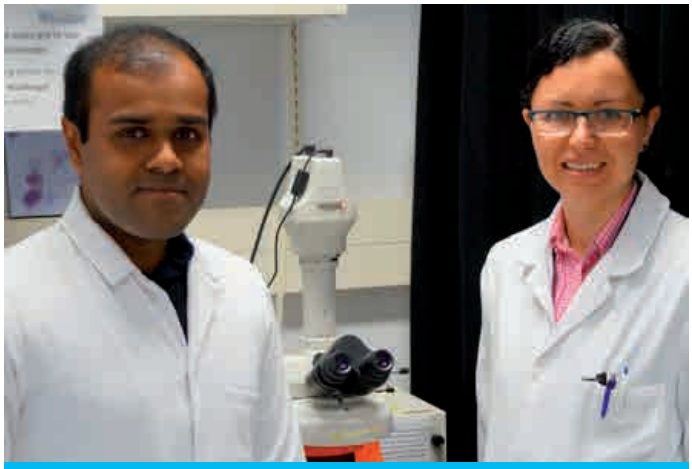
OTHER PRESTIGIOUS AWARDS

Year	Award	From	To
2015	Rutherford Medal	RSNZ	Ian Reid
2015	Liley Medal	HRC	Ian Reid
2015	Prime Minister's Science	NZ Gov't	Bone & Joint R G
2014	Research Excellence	UoA	Ian Reid
2012	Distinguished Professor	UoA	Ian Reid
2007	Gluckman Medal	UoA	Ian Reid

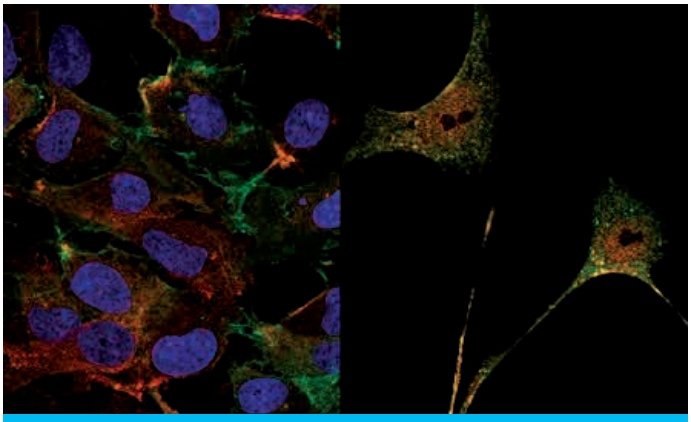
Professor Jillian Cornish and Distinguished Professor Ian Reid in their laboratory, circa 2006. (Photo courtesy of HRC)

An AMRF Success Story

INTRODUCING: KARAN GOVINDPANI, 2016 RECIPIENT OF THE AMRF BRIAN DE LUEN DOCTORAL SCHOLARSHIP



Mr Karan Govindpani with his PhD supervisor Dr Andrea Kwakowsky



Visualisation of vascular markers on human cerebral microvascular endothelial cells (left) and human temporal cortex pericytes (right) by fluorescence immunocytochemistry

I am a graduate of the University of Auckland, with a BSc (Hons) in Biomedical Science.

I am currently undertaking a doctoral research project in the Centre for Brain Research at the University of Auckland, with my research focusing on the study of the cerebral vasculature and its dysfunction in Alzheimer's disease. I am keenly interested in the study of human neurodegenerative disorders, and in particular the factors underlying disease pathogenesis and the identification of targets for the development of novel drugs and therapies. In the next few years, I aim to develop and expand my skills and knowledge, enabling me to make a meaningful contribution to this important and fascinating area of medical research.

The 2016 AMRF Brian De Luen Doctoral Scholarship has been invaluable to my progress this year.

I had initially embarked on this project without a scholarship, and it was a challenge to balance my research commitments with external work. The very generous award of a stipend for living expenses and the payment of tuition fees has allowed me to devote my attention fully to my research project, which has made a significant difference to the progression of my doctoral research. In addition to this, the funding towards research costs has significantly contributed to the experimental costs of the project. This scholarship has greatly aided in the realisation of my research goals, and a publication based on this work is currently in preparation. The travel grant provided by AMRF will make it possible for me to travel overseas to present this work at conferences and meet other researchers working in my field. Thus, I am very grateful for the award of the AMRF Brian De Luen Doctoral Scholarship, for contributing so much to my research and career development throughout my PhD.

"In carrying out this research into factors underlying the development of Alzheimer's disease, this work will make a significant contribution to the understanding on this disease, and possibly to the design of treatment strategies to combat its rising prevalence in the population. We are delighted and honoured to receive support from the Auckland Medical Research Foundation. The Brian De Luen Doctoral Scholarship allowed us to carry on this exciting work and it is crucial supporting and developing a promising young scientist like Karan."

Dr Andrea Kwakowsky, Karan's PhD supervisor

INTRODUCING: JENNIFER WELLER'S RESEARCH IN IMPROVING TEAM COLLABORATION IN THE OPERATING THEATRE

A MORSim simulation underway

Another simulation underway in the operating theatre

Associate Professor Jennifer Weller's research focuses on communication and teamwork within clinical environments.

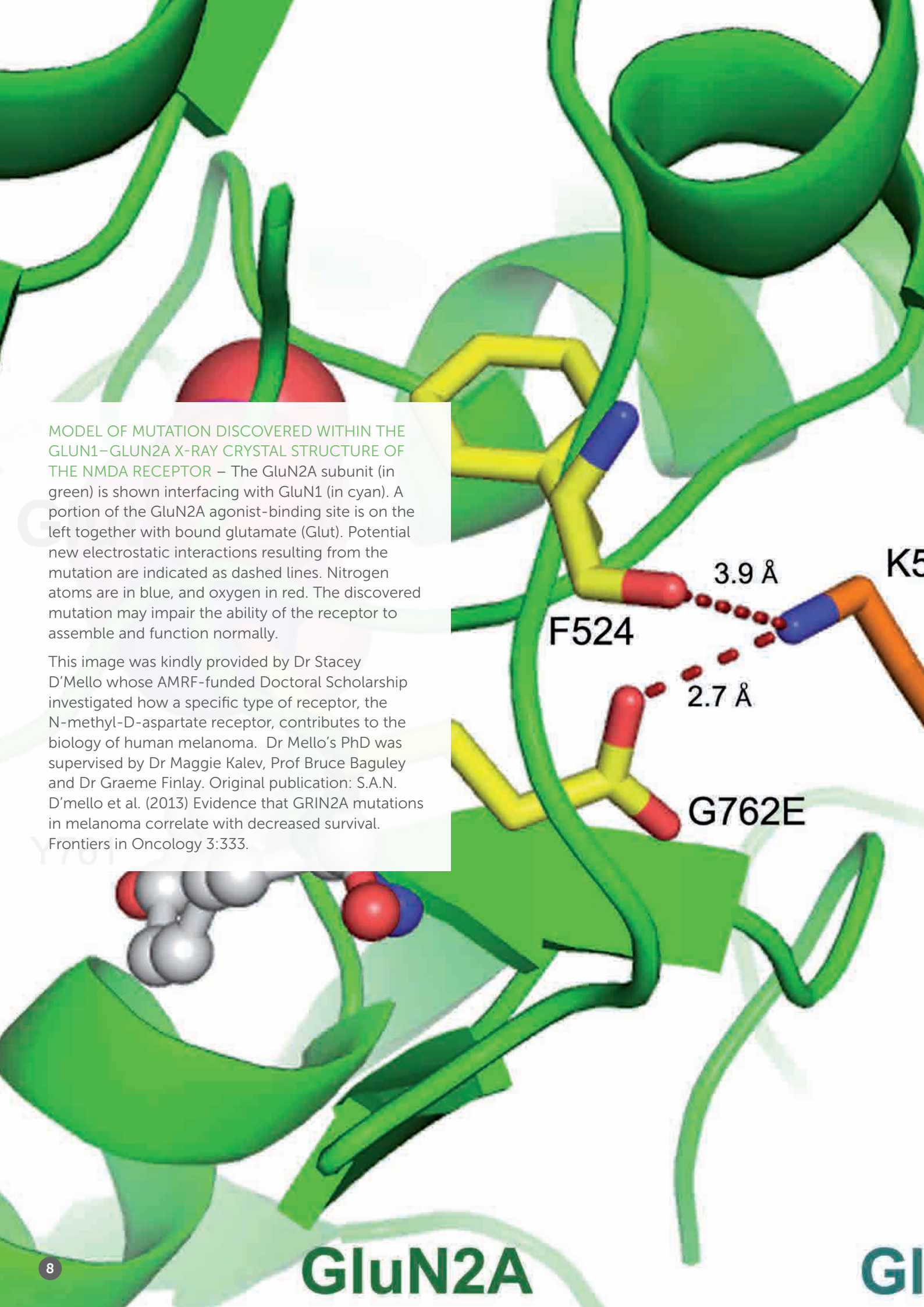
This year, her team completed their AMRF project grant titled 'Improving Team Collaboration in the Operating Theatre'. The Multidisciplinary Operating Room Simulation (MORSim) project was designed to be a course for teams of operating room staff to train together and improve teamwork. The course consisted of three simulated surgical cases with debriefs and lectures. A special effects company helped to make the simulations realistic and the course was administered at the University of Auckland Simulation Centre for Patient Safety. A total of 20 course days were run with 120 staff, including surgeons, anaesthetists, and nurses. The vast majority of participants said the training day was useful and almost 90% said they would change their practice as a result. There was a significant improvement in communication and information sharing over the course day and improved teamwork behaviours were also observed in the clinical environment.

"Funding from the AMRF was pivotal in the success of the pilot study. This has led to an Accident Compensation Commission contract of $4.8 million over the first 2 ½ years and expectations of a similar amount in the subsequent 2 ½ years to deliver MORSim training to every DHB in New Zealand."

Associate Professor Jennifer Weller, lead investigator, MORSim.

From left to right: Professor Alan Merry, Professor Ian Civil, Dr Jane Torrie, Associate Professor Jennifer Weller, Dr Craig Webster, Kaylene Henderson, Dr David Cumin

MORSim
Multidisciplinary
Operating Room Simulation

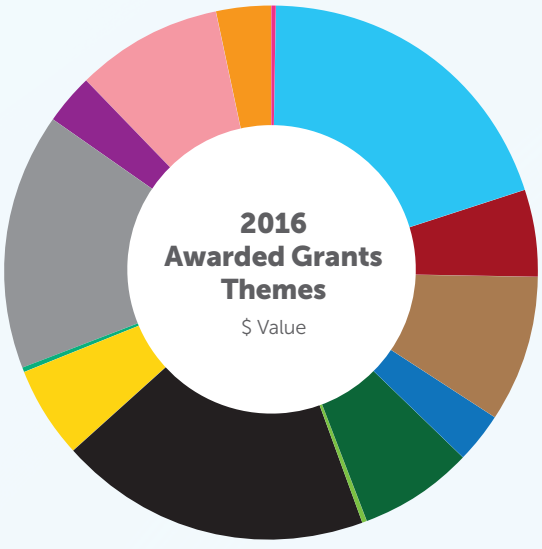


MODEL OF MUTATION DISCOVERED WITHIN THE GLUN1–GLUN2A X-RAY CRYSTAL STRUCTURE OF THE NMDA RECEPTOR – The GluN2A subunit (in green) is shown interfacing with GluN1 (in cyan). A portion of the GluN2A agonist-binding site is on the left together with bound glutamate (Glut). Potential new electrostatic interactions resulting from the mutation are indicated as dashed lines. Nitrogen atoms are in blue, and oxygen in red. The discovered mutation may impair the ability of the receptor to assemble and function normally.

This image was kindly provided by Dr Stacey D'Mello whose AMRF-funded Doctoral Scholarship investigated how a specific type of receptor, the N-methyl-D-aspartate receptor, contributes to the biology of human melanoma. Dr Mello's PhD was supervised by Dr Maggie Kalev, Prof Bruce Baguley and Dr Graeme Finlay. Original publication: S.A.N. D'mello et al. (2013) Evidence that GRIN2A mutations in melanoma correlate with decreased survival. Frontiers in Oncology 3:333.

GRANTS AWARDED

58 Grants Awarded Totalling $3,626,944



- Biomedical Imaging (1) | $3,000 0.08%
- Cancer (12) | $721,448 19.89%
- Cardiovascular Science (4) | $194,835 5.37%
- Cellular and Molecular Biology (4) | $321,472 8.86%
- Endocrinology, Metabolism and Nutrition (2) | $111,702 3.08%
- Infection and Immunity (4) | $259,926 7.17%
- Musculo-skeletal Science (1) | $2,112 0.06%
- Neuroscience (14) | $690,049 19.03%
- Other (3) | $203,824 5.62%
- Population Health (1) | $3,000 0.08%
- Reproduction, Development, Maternal and Newborn Health (5) | $558,966 15.41%
- Sensory Sciences (3) | $110,728 3.05%
- Surgery (3) | $325,882 8.99%
- Stem Cell Biology (1) | $120,000 3.31%

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

Grants Awarded

PROJECTS

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

Dr Jonathan Astin
Dept. of Molecular Medicine & Pathology, University of Auckland

The lymphatic vasculature plays an essential role in fluid homeostasis; it collects excess interstitial fluid and returns it to the bloodstream. Lymphatic vessel dysfunction leads to the painful and debilitating build-up of fluid in the body, termed lymphoedema. Secondary lymphoedema can occur when lymphatic vessels are damaged following the surgical removal of lymph nodes in cancer patients and it is one of the most significant survivorship issues following surgical or radiological treatment of tumours, particularly breast cancer. In New Zealand, 20% of women who undergo axillary lymph node removal and/or radiotherapy as part of treatment for breast cancer will develop secondary lymphoedema. There is no definitive cure for secondary lymphoedema and symptoms are managed through the wearing of compression garments, lifestyle changes and surgical removal of tissue. Consequently, there is considerable interest in therapies that stimulate lymphatic vessel repair to help prevent lymphoedema. However, we know very little about how lymphatic vessels regenerate following injury. In this project we will develop new models of lymphatic vessel repair and use these to identify the mechanisms and genes involved in lymphatic regeneration. This work will be an important first step in the development of new therapies in the prevention of secondary lymphoedema.

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

Atrial fibrillation is an abnormal heart rhythm, which is common in older people. It is associated with increased risk of stroke, which can have devastating consequences. Patients who have episodes of atrial fibrillation frequently receive anticoagulant medicines (such as warfarin) to reduce the risk of stroke. After surgery, it is common for older patients to have an episode of atrial fibrillation. We do not know how commonly this occurs, or what the consequences are. The Perioperative Atrial Fibrillation and Postoperative Stroke (PAFS) study will determine the incidence and consequences of atrial fibrillation after surgery. Patients will wear a heart monitor before surgery, and for two weeks after surgery. They will undergo MRI scan of their brain several days after surgery looking for any evidence that they have had a small stroke. This study will be performed across several hospitals internationally, including Auckland City Hospital. The PAFS study might change how we treat patients who have an episode of atrial fibrillation after an operation, in order to protect them from complications such as stroke.

FUNDED BY: AC Horton Estate

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

Prof Larry Chamley, Dr Scott Graham
Dept. of Obstetrics & Gynaecology, University of Auckland

Extracellular vesicles are part of an elaborate system that the fetus uses to control maternal blood pressure as well as the maternal immune system during pregnancy. Antiphospholipid antibodies are found in some women and cause still-births and recurrent miscarriages. These antibodies also increase the chance that a woman will develop potentially fatal high blood pressure during pregnancy. We have previously shown that antiphospholipid antibodies can change the nature of placental vesicles such that they might cause increased blood pressure and other complications of pregnancy. In this study we will examine the maternal organs, and the cells within those organs, that placental vesicles target. We will also investigate whether treating placentas with antiphospholipid antibodies alters which maternal organs placental vesicles target to. This research will help us to understand how the fetus controls its mother's physiological systems by targeting specific maternal organs to allow normal pregnancies and whether inappropriate targeting of placental vesicles causes diseases of pregnancy.

MEASURING IN VIVO ACTIVITY IN THE AUDITORY CORTEX AND ITS LINK TO AUTISM SPECTRUM DISORDERS ($159,250 - 2 years) 1116009

Dr Juliette Cheyne, Prof Peter Thorne, A/Prof Johanna Montgomery
Dept. of Physiology & Centre for Brain Research, University of Auckland

Autism Spectrum Disorders (ASD) are developmental disorders defined by learning difficulties, sensory issues, communication difficulties, social deficits and stereotyped behaviours. Because ASD symptoms appear during infancy, it is crucial to examine how brain development is altered, as this could cause behavioural deficits. The social and communication difficulties in ASD are thought to be due to abnormalities in the processing of sounds, which in turn impairs language abilities. We hypothesise that this impaired sound processing is due to connections between brain cells in the auditory cortex forming incorrectly during development. We will utilise state-of-the-art cellular recording techniques in live mice to determine how the development of the auditory cortex is affected in ASD. We will reveal developmental differences in brain activity in ASD mice, which could lead to deficits later in life. We will also determine whether cortical organisation of tones (from high to low frequency) and plasticity in the auditory cortex are altered in ASD mice. The information obtained in this study is essential to advance knowledge of how changes in the activity in the developing brain link to deficits in sensory processing later in life, which could also be relevant to other neurodevelopmental disorders.

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

A/Prof Brent Copp, Prof Jean Michel Brunel, Dr Siouxsie Wiles
School of Chemical Sciences, University of Auckland

For several decades the routine use of antibiotics has saved countless lives. Recently, the World Health Organisation described how antibiotic-resistant bacteria are present in every region of the world, including New Zealand, and called for drastic action to prevent a return to the pre-antibiotic era. New antibiotics are needed, or alternatively, new methods are needed to restore the activity of antibiotics against drug-resistant bacteria. We have recently discovered a class of compounds that do the latter – enhancing the activity of the antibiotic doxycycline towards the normally drug resistant bacterium Pseudomonas aeruginosa. This project involves the synthesis and biological evaluations of new molecules based around our discovery, where we will optimise the antibiotic enhancing activity of this compound class and determine how such enhancement is achieved. This will provide proof of concept as to whether such compounds can be used to 'rehabilitate' old antibiotics, and to thereby restore their effectiveness to aid in the fight against drug-resistant bacterial infections.

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

Dr Justin Dean, Prof Alistair Gunn
Dept. of Physiology, University of Auckland

In New Zealand, approximately 500 babies are born prematurely every year, and around half survive with life-long disabilities. These disabilities often result from infection and inflammation around the time of birth. Excitingly, we now know that the brains of preterm babies can recover rapidly from injury, but may then fail to develop normally. Using a new rodent model of very preterm brain injury, we found that inflammation can impair normal brain development. Further, this was associated with a reduction in the levels of insulin-like growth factor (IGF-1), a molecule critical for normal brain growth. In this proposal, we will test whether restoring normal levels of IGF-1 in the brain during or after infection will promote brain maturation, and thus restore normal brain development. We will compare direct treatment of the brain using IGF-1 with an agent that can improve availability of locally produced IGF-1.

FUNDED BY: NR Thompson Trust

CLINICAL PROGNOSTIC MODELS IN BREAST CANCER ($72,423 - 1 year) 1116017

Prof Mark Elwood, Prof Ross Lawrenson, Dr Sandar Tin Tin, A/Prof Vernon Harvey, A/Prof Ian Campbell
Epidemiology and Biostatistics, School of Population Health, University of Auckland

This project will develop and assess methods to predict future outcome for women treated for breast cancer. We will use the information in the combined Auckland-Waikato breast cancer registries, provided by over 7000 women with at least 5 years' follow-up from diagnosis; we will develop a New Zealand-specific system to predict breast cancer outcomes, and compare its performance with existing methods, which have all been developed overseas. Such a model will use data collected routinely in current clinical practice, and will be applicable to individual patients, particularly to identify those with likely very good or very poor outcomes.

FUNDED BY: Hugh Green Fund

REGULATION OF DOPAMINE RELEASE BY ENDOCANNABINOIDS ($150,019 - 2 years) 1116016

Dr Peter Freestone, Prof Janusz Lipski
Dept. of Physiology, University of Auckland

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. I recently discovered that a unique cannabis-like substance produced in the brain (an endocannabinoid) – NADA – can alter the activity of dopamine-producing cells. This particular endocannabinoid is of great interest as it shares a common biosynthesis pathway with dopamine and is therefore of high importance to the pathophysiology of Parkinson's disease. The current study will use advanced dopamine-detection (electrochemistry) and cell-type specific stimulation (optogenetics) techniques that are ideally suited to studying the complex network underlying dopamine release. These approaches will establish the mechanism by which NADA controls dopamine levels and related movement behaviours. A range of experimental models from living brain slices to freely moving animals will be used to provide a robust translational investigation. The findings will determine whether the NADA-based mechanism is a suitable target for new therapeutic strategies for diseases like Parkinson's disease – "The saddest of diseases" (James Parkinson 1817).

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

A/Prof Michelle Glass, Dr Scott Graham, Dr Graeme Finlay
Dept. of Pharmacology & Clinical Pharmacology, University of Auckland

While there is a public perception that cannabis might cure cancer, the scientific evidence is far from clear cut. Cannabis itself is made up of a number of different compounds, but the key psychoactive ingredient targets a receptor in the brain called CB1. CB1 has been under investigation for a number of years as a possible therapeutic target, and there are now many compounds available that can activate or inhibit this receptor. In studies investigating cannabinoid ligands that target the cannabinoid receptors in cancer cells the outcome has been quite mixed, with some reports of tumour cell death, but others that have observed an increase in cell proliferation. We have some evidence

Grants Awarded continued

to suggest that the level of cannabinoid CB1 receptors expressed in cells influences the signal that is produced by activation of the receptors – and hypothesise that this observation is the reason for the diverse findings in the field. Here we aim to utilise human brain cancer cells to investigate if the expression and function of cannabinoid receptors in these cells and determine if CB1 receptors are a valid therapeutic target.

FUNDED BY: Pauline Gapper Charitable Trust

INVESTIGATION OF TRIM28-KRAB INTERACTIONS ($158,200 - 2 years) 1116014

Dr David Goldstone
School of Biological Sciences, University of Auckland

Mammalian genomes are littered with the remains of previous retroviral infections. During the early stages of development these retroviral sequences are potently and permanently silenced preventing the expression of retroviral genes. This silencing accompanies the wave of differentiation that alters transcription during normal development and acts to shape the genes that are expressed in particular cells. Trim28, a member of the tripartite motif protein family, is the central player in this control and as such has been labelled the master regulator of the human genome. More recently Trim28 has been implicated in cancer, diabetes and obesity. We aim to understand the molecular details that target Trim28 to particular sites within the genome resulting in the silencing of particular genes. This research will lay the foundation to manipulating this system to alter transcription and treat diverse medical diseases.

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, University of Auckland

Some cancer patients who are treated with 5-FU, and other related drugs, have an increased chance of treatment failure due to high expression of the drug target (thymidylate synthase). An inherited risk for poor treatment outcome has been reported in a number of studies. It is possible to look at a patient's DNA to see if they have this thymidylate synthase gene variant. But currently when these individuals are identified there is no clear way to decide how to safely and appropriately increase the drug dose. Our project will assess a method of monitoring effective 5-FU concentrations at the drug target in the cell. We want to adapt and improve the method using a technique called targeted peptide analysis. If this test is sensitive, accurate and reproducible enough we may then be able to use this approach to help oncologists to improve the safe and effective use of this drug especially in those people who may have inherited a resistance to this type of treatment.

FUNDED BY: Anonymous Donor

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, University of Auckland

Minimally invasive procedures provide a real alternative to surgical resection for small tumours. Success of the technique depends largely on the accuracy of ablation probe placement for killing tumour cells in situ, while also limiting damage to healthy tissue. However, 2D ultrasound image based guidance of a probe, as used in current clinical practice, does not provide precise 3D information of the probe tip, therefore the errors need be corrected to have an optimal operational outcome. We propose to develop an Augmented Reality aided navigation system which is delivered through a Head Mounted Display (HMD). We aim to accomplish four tasks over a two-year timeframe: (1) To develop a vision-driven abdominal model incorporating respiration effects; (2) To integrate data from vision and motion sensors for improved accuracy of probe placement; (3) To implement an Augmented Reality environment delivered through a HMD; and (4) To validate the algorithms using a 4D ultrasonic scanner and an abdominal phantom. Successful implementation of the workflow will not only lead to new methods for precise positioning of ablation probes, but will also establish cornerstones for the use of Augmented Reality in a clinical environment in New Zealand.

FUNDED BY: W & WAR Fraser Charitable Trust

NIVORAD ($104,454 - 2 years) 2116019

Dr Louis Lao, Dr George Laking
Radiation Oncology, Auckland District Health Board

This study aims to evaluate whether addition of stereotactic radiotherapy provides additional benefit in patients who are treated with immunotherapy (nivolumab) for advanced lung cancer. Immunotherapy is a treatment which helps a person's immune system to fight cancer. Nivolumab have generated a lot of interest recently having made major breakthroughs in cancer patients. Stereotactic radiotherapy is a type of radiotherapy where very large doses are given very precisely. While radiotherapy has been used as a cancer therapy for a long time, there is now interest in the idea that radiotherapy can have immunological effects and that it can enhance the effects of immunotherapy. This study will look at this new treatment concept of combining immunotherapy with stereotactic radiotherapy to better understand its effectiveness and also safety. Both immunotherapy and stereotactic ablative radiotherapy are state-of-the-art cancer treatments which have changed the landscape of cancer treatment in recent years. In New Zealand, access to these types of treatment is limited. This study will allow New Zealand patients access to these types of treatment and help to

answer an important scientific question which potentially will translate into a new treatment paradigm which will help to improve patient's outcomes.

FUNDED BY: Anonymous Donor

CYSTINE/CYSTEINE REDOX SIGNALLING IN THE AGING EYE ($106,260 - 2 years) 1116006

Dr Julie Lim, Prof Paul Donaldson, Dr Monica Acosta
Dept. of Physiology, University of Auckland

With advancing age, oxidative stress results in redox imbalance and eye diseases which threaten the sight of the elderly. We propose that the cystine/glutamate antiporter (CGAP) in the eye is important for maintaining redox balance and minimising oxidative stress. Clinical assessments on CGAP knockout mice reveal the early onset of eye diseases. To elucidate the underlying pathways that result in these pathologies, molecular and functional tests will be performed and this information used to guide the design of effective therapies that target a specific tissue of the eye against oxidative stress to delay the onset of age-related eye diseases.

FUNDED BY: John Jarrett Trust

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

Dr Rinki Murphy, Ms Naomi Davies, Dr Justin O'Sullivan, A/Prof Lindsay Plank
Dept. of Medicine, University of Auckland

The prevalence of diabetes has reached epidemic proportions in New Zealand, with reported prevalence at 7% among adults. Bariatric surgery is currently the only therapy with long-term weight reduction and dramatic effects on both remission and prevention of type 2 diabetes among those with severe obesity. Currently, the most improved rates of diabetes remission are being reported in patients receiving gastric bypass (GBP) compared to sleeve gastrectomy (SG). Therefore, understanding the mechanisms underlying the distinct and common impacts of GBP over SG in achieving type 2 diabetes remission and sustained weight loss is important for developing novel medical treatments. Gut hormones and microbiota, are emerging as novel mediators of obesity and type 2 diabetes. They play a key role in dietary energy extraction, hunger stimulation, inflammation, glucose metabolism and improved metabolic outcomes. This research aims to determine how the two main bariatric surgery procedures, GBP and SG, induce changes in gut microbiota, how these changes relate to the fluctuation of gut hormones, and how this differs between the contrasting surgeries. This work has the potential to identify novel probiotics or a gut microbiota transplant strategy for management of obese patients with type 2 diabetes to complement or replace surgery.

HORMONAL MARKERS OF DIABETES AFTER ACUTE PANCREATITIS ($108,702 - 2 years) 1116021

Dr Max Petrov, Dr Rinki Murphy
Dept. of Surgery, University of Auckland

The project aims to define new onset diabetes after diseases of the exocrine pancreas, more specifically acute pancreatitis, and to characterise its underlying hormonal profile. One of the key objectives is to test the hypothesis that a blunted pancreatic polypeptide response to a mixed-nutrient meal test is a specific marker of diabetes after acute pancreatitis (compared to type 2 diabetes mellitus). Additionally, we seek to characterise patterns of insulin secretion and resistance as well as gut hormonal (incretin) response in these two diabetes subtypes (type 2 diabetes mellitus and diabetes after acute pancreatitis). It is envisaged that data generated from this project will enable earlier diagnosis and better treatments for diabetes after diseases of the exocrine pancreas, for which there are no specific guideline recommendations.

FUNDED BY: Marion Ross Memorial Fund

EPIGENETICS OF PROGESTERONE RESISTANCE IN ENDOMETRIOSIS ($157,141 - 2 years) 1116005

Dr Anna Ponnampalam, Prof Cynthia Farquhar
Liggins Institute, University of Auckland

Endometriosis is characterised by the presence and growth of endometrium (the lining of the uterus) outside the uterus. It is a common cause of infertility and chronic abdominal pain in reproductive-age women. While the incidence is approximately 10%, the actual prevalence is much higher because many women and girls are initially misdiagnosed. Endometriosis-related pain is serious, debilitating and episodic. Current treatment modalities have major limitations and are only successful in half the patients and these women generally develop resistance to repeated treatments with the same agent over a period of 6 months to 3 years. Hence the clear need to identify novel molecular pathways that can provide early identification of developing resistance, inform current therapies and enable future targeted therapy development. The project is to test the hypothesis that DNA methylation plays a crucial role in the aberrant oestrogen priming of the endometrium that led to progesterone resistance and development of endometriosis. The overall objective of this project is to understand the mechanisms involved in progesterone resistance generally seen in endometriosis, thereby improving identification and potentially enabling the development of effective therapeutic interventions.

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

Dr Fiona Radcliff, A/Prof Thomas Proft
Dept. of Molecular Medicine & Pathology, University of Auckland

Effective delivery of approved vaccines typically requires qualified personnel, defined storage conditions and injection of the materials. Using live organisms, such as food-grade bacteria, for vaccine production and needle-free delivery (eg by ingestion) is a promising alternative. A novel vaccine delivery vehicle, called PilVax, has been developed by researchers at the University of Auckland. The basis of PilVax is a bacterium found in yoghurt,

Grants Awarded continued

called Lactococcus lactis, which has been modified to express large quantities of foreign proteins, including vaccine candidate antigens, on its surface. Preliminary studies in mice have shown that delivery of PilVax into the nasal cavity can indeed stimulate robust immune responses. The goal of this project is to build on that work by testing whether PilVax mediated delivery of vaccine candidate antigens from Staphylococcus aureus, an important bacterial pathogen that is very common in New Zealand, can stimulate protective immunity to this pathogen. If PilVax proves to be effective in these tests it will establish this delivery platform as a promising and flexible approach for non-invasive vaccination against not only S. aureus but also other mucosal pathogens.

FUNDED BY: John and Poppy Stilson Endowment Trust

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HNF1B-ASSOCIATED DISEASE IN A HUMAN KIDNEY ORGANOID MODEL ($120,000 - 1 year) 1116018

Dr Veronika Sander, A/Prof Alan Davidson, Dr Rinki Murphy
Dept. of Molecular Medicine & Pathology, University of Auckland

Kidney disease is a serious problem in New Zealand, particularly amongst the Māori and Pacific people. Cystic kidney disease is common and is associated with the progressive growth of fluid-filled cysts that can eventually cause kidney failure. Mutations in the HNF1B gene, which acts as a "master switch" for many other kidney genes, are responsible for cyst formation but the molecular pathways operating downstream of HNF1B are poorly understood. Furthermore, there is no good way to study human kidney cyst formation in the laboratory. We have established state-of-the-art strategies that allow us to grow human kidney organoids (cultured mini kidneys) and introduce HNF1B mutations into these cells. This novel approach provides a new tool to study kidney cyst formation and, in future applications, will enable new drugs to be tested.

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

Dr Giuseppe Sasso, Dr Shankar Siva, Mrs Rebecca Montgomery
Radiation Oncology, Auckland District Health Board

Stereotactic ablative body radiotherapy (SABR) is a high-precision, non-invasive and low-toxicity alternative for treatment of small lung lesion. Due to early reports of excellent control rates (comparable to surgery) and minimal associated toxicities, SABR is being rapidly implemented worldwide and in New Zealand in the treatment of small peripheral lung lesions. Approximately 30% of all cancer patients will develop secondary spread to the lung during the course of their disease. In patients with limited secondary cancer in the lung, SABR can result in long-term survival and even cure. As it is non-invasive, delivered in as little as a single outpatient visit and without the need for hospitalisation, SABR is an attractive and potentially very cost-effective treatment option. Additionally, emerging evidence suggests that large doses of precision SABR may evoke a strong immune response to recognise and attack remaining tumour cells in the body. SAFRON II is a randomised phase II clinical trial comparing single treatment versus multi-treatment SABR techniques (ie 4 fractions). This research will be the first comprehensive evaluation of SABR techniques integrating the assessment of (1) clinical outcomes, (2) quality of life, (3) cost-efficacy and (4) translational immunological investigation.

EPIGENETIC TARGETING OF METASTASIS ($106,725 - 2 years) 1116002

Dr Dean Singleton, A/Prof Adam Patterson
Auckland Cancer Society Research Centre, University of Auckland

Breast cancer is the most common cancer in New Zealand women accounting for nearly 3,000 new registrations and over 600 deaths each year. Although breast cancer outcomes are improving with earlier detection and more effective treatments, most patients die when their cancers spread (metastasise) into secondary organs. The blood vessels that supply breast tumours are poorly developed and are unable to deliver sufficient oxygen to the tumour. This results in regions of low oxygen (hypoxia) forming within the tumour. Hypoxia is critically important because it causes cancer cells to become more invasive, resulting in an increased risk of metastasis and poorer patient survival. This occurs because certain enzymes sense low oxygen and respond by switching on genes that promote invasion. We are developing new drugs to target these changes. In this work we will investigate the potential of these drugs to prevent hypoxia signalling in tumour models and reduce tumour growth and metastasis. The results of this study will help to develop effective strategies to prevent cancer metastasis and improve patient survival.

FUNDED BY: Anonymous Donor

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

Dr Clinton Turner, Prof Mike Dragunow, A/Prof Maurice Curtis
Anatomical Pathology, Auckland District Health Board

Meningiomas are tumours of the covering layer (the dura) of the central nervous system. In New Zealand it has been reported that these tumours disproportionately affect Maori and Pacific Island women – who appear to get meningiomas at a younger age and have tumours that are larger in size than Caucasians. While the majority of meningiomas are "benign", they may still cause significant harm by growing in critical locations or surgically inaccessible sites thereby preventing complete removal. Some meningiomas may also repeatedly recur, necessitating repeated surgical intervention and/or radiotherapy. Compared to many other tumours, meningioma research is a relatively

neglected area. The role of the immune system has been widely investigated in a variety of tumours (eg melanoma, breast cancer). This has resulted in the realisation that the tumour-associated immune cell infiltrate is often highly prognostically significant. The goal of this research is to examine whether the composition and density of the immune cell infiltrate in meningioma is prognostically significant in predicting tumour recurrence. This will potentially help improve the ability of the pathologist to predict tumour behaviour for an individual patient. It may also open up further research avenues into immune-modifying therapies in meningioma.

miRNAS AS EARLY PREDICTORS OF PRETERM BIRTH
($114,379 - 2 years) 1116010

A/Prof Mark Vickers, Prof Lesley McCowan, Dr Katie Groom, Dr Clint Gray
Liggins Institute, University of Auckland

At a global level, more than one in 10 babies are born too early (<37 weeks of pregnancy) equating to over 15 million preterm births and more than one million new-born deaths. Preterm birth also increases the risk of death due to other causes including neonatal infections. In New Zealand, nearly 8% of babies are born preterm and, of those, approximately 60% occur after spontaneous onset of labour. Preterm birth rates are higher in Maori women at around 14%. Although women with a previous spontaneous preterm birth (SPTB) are considered to be at high risk for recurrence, the majority occur in women without prior history. Accurate prediction of SPTB risk, before the clinical event, would allow for improved care and the potential for targeting novel and existing therapies to prevent SPTB, which may result in improved outcomes for both infant and mother. We have preliminary data showing that miRNA signatures in maternal blood as early as 20 weeks gestation can differentiate between those that go on to deliver at term or experience early SPTB (28-32 weeks). This project will expand on these findings to work towards development and validation of effective non-invasive biomarkers to identify women at risk for SPTB.

FUNDED BY: Rotary Club of Auckland Harbourside, Inc

DOCTORAL SCHOLARSHIPS

RISK ASSESSMENT FOR EMERGENCY LAPAROTOMY
($128,000 - 3 years) 1216005

Dr Ahmed Barazanchi
South Auckland Clinical School, University of Auckland

Emergency laparotomy is a commonly performed surgical procedure with a high mortality and morbidity. Several different operations can be classified as an emergency laparotomy and it is commonly performed on acutely unwell patients as a lifesaving procedure. Predicting outcomes preoperatively is paramount for patient information, planning of perioperative care and deciding on palliative therapies. This study aims to develop a reliable, easy-to-use predictive score based on preoperative patient state. The score will be developed using a retrospective review of Middlemore Hospital patients over the last ten years. The score will be validated and adjusted based on prospective multicenter cohort study run for one year and three months. The risk score will also aim to follow up patients for one year to predict long term impact in the form of ongoing morbidity and quality of life. The risk assessment score will be introduced into a clinical pathway for emergency laparotomy patients. The clinical pathway will provide appropriate level care for high risk patients to reduce overall mortality and morbidity. The proposed study will be the first New Zealand developed emergency laparotomy scoring system. The scoring system will also be the first developed prospectively specifically for emergency laparotomies.

BARBARA BASHAM DOCTORAL SCHOLARSHIP

EXPLOITING BRAIN MECHANISMS TO PROTECT THE PRETERM BRAIN FROM INJURY
($128,000 - 3 years) 1216004

Mr Hyeon Tae (Kenta) Cho
Dept. of Physiology, University of Auckland

Many preterm infants develop brain injury around the time of birth, with a high risk of life-long disability. Currently, we have no effective way of preventing disability. Our preliminary findings using a well-established animal model of preterm brain injury suggest for the first time that therapeutic manipulation of a critical endogenous, neuroprotective, anti-inflammatory mechanism can reduce damage to oligodendrocytes, the myelin-producing cells of the CNS. These findings suggest that it is possible to preserve myelination by supporting natural pathways in the brain. However, it remains to be proved whether this therapy will be effective when used at clinically relevant times, with the inevitable delays between injury and initiation of therapy. Thus, to replicate and extend our findings we will robustly test the optimal "window of opportunity" during which this therapy might be instituted to rescue these cells from irreversible damage or cell death.

FUNDED BY: Barbara Basham Medical Charitable Trust

BRIAN DE LUEN DOCTORAL SCHOLARSHIP

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

Mr Karan Govindpani
Dept. of Anatomy and Medical Imaging, University of Auckland

Alzheimer's disease (AD) is a common neurodegenerative disorder, and the leading cause of dementia in elderly

Grants Awarded continued

patients. It is well-known that the brain vasculature is severely affected in AD, often years to decades before the appearance of clinical symptoms. Pericytes are cells that wrap around small blood vessels in the brain, causing them to expand or contract to change blood flow. The neurotransmitter γ-aminobutyric acid (GABA) is present at high levels in the healthy brain and has a range of important functions, including the regulation of neuronal excitability. However, the GABA system may become dysfunctional in AD. Since GABA regulates blood flow, we are interested in determining whether GABA may exert this role through contractile pericytes. In this study, we will attempt to detect and locate components of the GABA neurotransmitter system in pericytes and other cells of the brain circulatory system, and to study whether these are altered in AD. In addition, we will test the responses of pericytes to drugs that target the GABA system, with the aim of trying to compensate for changes that we might detect in AD. This research will help to determine whether GABA dysfunction contributes to vascular changes in AD.

FUNDED BY: Brian De Luen Estate

CORTICAL EXCITATION-INHIBITION BALANCE IN HEALTH AND DISEASE ($87,000 - 2 years) 1216006

Ms Rachael Sumner
Dept. of Psychology, University of Auckland

Despite the widespread prevalence of depression, currently accepted treatments do not work for approximately one-third of patients. One of the key reasons for this is that there remains a fundamental lack of understanding of the biological basis and causes of depression. Continuing advancement in brain imaging techniques provide potentially valuable new methods for measuring biomarkers of central nervous system diseases. Biomarkers can potentially be used for understanding the causes of diseases and for the prediction and evaluation of treatment outcomes. The application of brain imaging techniques for measuring biomarkers of depression will allow new mechanistic insights into the disease process that has not been possible in the past. The main aim of this research is to investigate the use of electroencephalography (EEG) to measure biomarkers of cortical excitation/inhibition and neural plasticity in depression. Reduced neural plasticity has been implicated in a number of brain based disorders, including depression. By targeting visual and auditory evoked neural activity this project will explore how measuring changes in sensory neural plasticity could be used as biomarkers of general brain health in depression.

FUNDED BY: NH Taylor Charitable Trust

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POSTDOCTORAL FELLOWSHIP

EDITH C COAN RESEARCH FELLOWSHIP

ENDOSCOPIC MAPPING OF GASTRIC SLOW WAVES ($199,473 - 2 years) 1316001

Dr Timothy Angeli
Auckland Bioengineering Institute, University of Auckland

The mechanical contractions that are responsible for breaking down and transporting food through the gastrointestinal (GI) tract are initiated and coordinated by underlying bioelectrical events, termed "slow waves." In the healthy stomach, slow waves propagate in a routine, highly-organised pattern down the stomach. Abnormal slow wave patterns, termed "dysrhythmias," have been associated with many digestive disorders, where patients suffer frequent debilitating symptoms including abdominal pain, bloating, nausea, and vomiting. Diagnosis of digestive disorders can be difficult, causing frustration for patients and clinicians, and current approaches for detecting the spatially-complex GI dysrhythmias require surgery. To address this clinical problem, I aim to develop and validate endoscopic (down the throat) gastric electrical mapping as a minimally-invasive technique for diagnosing gastric dysrhythmias, where a custom-designed electrode array will be applied to the inside of the stomach to map slow wave activation patterns. A safe and effective approach for endoscopic delivery will be developed, and the accuracy of the endoscopic electrical recordings will be verified intraoperatively against highly-validated but surgically-invasive recordings. Finally, minimally-invasive gastric mapping will be validated in patients undergoing routine endoscopy. Altogether, this project has the potential to deliver a novel diagnostic approach for debilitating digestive disorders.

FUNDED BY: Edith C Coan Trust

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OTHER GRANTS AWARDED

DOUGLAS GOODFELLOW REPATRIATION FELLOWSHIP EXTENSION

$195,924 1413001-1

Dr Andrew Wood
Dept. of Molecular Medicine & Pathology, University of Auckland

1 year extension for his Douglas Goodfellow Repatriation Fellowship "Developing zebrafish *ETV6* models of acute myeloid leukemia (AML) for chemical suppressor screens"

FUNDED BY: Douglas Goodfellow Charitable Trust

KELLIHER CHARITABLE TRUST EMERGING RESEARCHER START-UP AWARDS

$30,000 1716001

Dr Petr Tomek
Auckland Cancer Society Research Centre, University of Auckland

Research support for his Edith C Coan Research Fellowship "The role of the protein IMPACT in survival of cancer cells during tryptophan deprivation"

FUNDED BY: Kelliher Charitable Trust

Kelliher Charitable Trust

$30,000 1716002

Dr Sandar Tin Tin
Epidemiology and Biostatistics, School of Population Health, University of Auckland

Research support for her David and Cassie Anderson Research Fellowship "National population-based study of gene mutation, genetic testing and targeted therapy in lung cancer".

FUNDED BY: Kelliher Charitable Trust

Kelliher Charitable Trust

HEALTHEX EMERGING RESEARCHER AWARDS

$3,000 Travel Award 6716001

Miss Grace Gong
Dept. of Molecular Medicine & Pathology, University of Auckland

To attend a conference to present her research in the field of cellular and molecular biology.

$2,000 Travel Award 6716002

Mr Hans Vellara
Dept. of Ophthalmology, University of Auckland

To attend a conference to present his research in the field of eye disease.

$2,000 Travel Award 6716003

Mr Maximilain Joret
Dept. of Pharmacology with Clinical Pharmacology, University of Auckland

To attend a conference to present his research in the field of neuroscience.

ALL HEALTHEX AWARDS **FUNDED BY:** Wellington Sisters Charitable Trust

with you for generations to come Trust

TRAVEL GRANTS AWARDED

Dr Emma Best
Dept. of Paediatrics; Child and Youth Health, University of Auckland

To attend the Infection and Immunity in Children course and Australia New Zealand Paediatric Infectious Diseases clinical meeting, Perth, Australia, 30 November – 2 December 2016.

Dr Sandra Bourke
Dept. of Medicine, University of Auckland

To attend the American College of Rheumatology (ACR) meeting, Washington DC, USA, 11 – 16 November 2016.

Dr Karen Brewer
Te Kupenga Hauora Māori, University of Auckland

To attend the Speech Pathology Australia National Conference, Perth, Australia, 15 – 18 May 2016.

Dr Julie Brown
Liggins Institute, University of Auckland

To attend the 2016 Annual Conference of the Perinatal Society of Australia and New Zealand, Townsville, Australia, 21 – 25 May 2016.

Dr Joanne Davidson
Dept. of Physiology, University of Auckland

To give an invited talk at the University of Gothenburg, Sweden and to attend the 2016 Hershey meeting in Paris, France, 2 – 12 June 2016.

Dr Victor Dieriks
Dept. of Anatomy with Medical Imaging, University of Auckland

To attend the Non-Motor Dysfunctions in Parkinson's Disease and Related Disorders (NMDPD), Ljubljana, Slovenia, 6 - 9 October 2016 and to visit collaborators in Belgium, 10 – 18 October 2016.

Dr Robert Galinsky
Dept. of Physiology, University of Auckland

To attend the 2016 Annual Conference of the Perinatal Society of Australia and New Zealand, Townsville, Australia, 21 – 25 May 2016.

Dr Youngchuan Gu
Auckland Cancer Society Research Centre, University of Auckland

To attend the 15th Human Proteome Organisation World Congress and related academic visits, Taipei, Taiwan, 15 September – 1 October 2016.

Dr Jian Guan
Dept. of Pharmacology & Clinical Pharmacology, University of Auckland

To provide partial support for travel to Europe for attending 3 conferences and 2 laboratory visits, Europe, 26 May – 26 June 2016.

A/Prof Michael Hay
Auckland Cancer Society Research Centre, University of Auckland

To attend the Tumour Microenvironment Conference 2016, Rhodes, Greece, 5 – 10 June 2016.

Dr Kimiora Henare
Auckland Cancer Society Research Centre, University of Auckland

To attend the World Indigenous Cancer Conference 2016, Brisbane, Australia, 11 – 17 April 2016.

Grants Awarded continued

Dr Rashi Karunasinghe
Dept. of Physiology, University of Auckland

To attend the 10th Federation of European Neuroscience Societies (FENS) forum of Neuroscience, Copenhagen, Denmark,
21 June – 6 July 2016.

Dr Julie Lim
Dept. of Physiology, University of Auckland

To attend the International Society for Eye Research, Tokyo, Japan,
24 September – 1 October 2016.

Professor Janusz Lipski
Dept. of Physiology, University of Auckland

To attend the Triennial International Dopamine Meeting, Vienna, Austria, and lecture at the Nencki Institute of the Polish Academy of Sciences, Warsaw, Poland, 5 - 23 September 2016.

Dr Sue McGlashan
Dept. of Anatomy with Medical Imaging, University of Auckland

To attend the Osteoarthritis Research Society International (OARSI) 2016 World Congress on Osteoarthritis, Amsterdam, The Netherlands, 1 – 4 April 2016.

Dr Kimberly Mellor
Dept. of Physiology, University of Auckland

To attend the Experimental Biology Conference 2016, San Diego, USA,
2 – 6 April 2016.

Dr Justin O'Sullivan
Liggins Institute, University of Auckland

To attend the 2016 FASEB Yeast chromosome structure, replication and segregation meeting, Snowmass, Colorado, USA, and to meet with collaborators, 31 July – 5 August 2016.

Dr Brigid Ryan
Dept. of Anatomy with Medical Imaging, University of Auckland

To attend the Neuroscience School of Advanced Studies conference/course and laboratory training at the Max Planck Research Unit for Neurogenetics, Sudtirol, Italy and Frankfurt, Germany, 20 August – 2 September 2016.

Dr Anna Serlachius
Dept. of Psychological Medicine, University of Auckland

To attend the International Congress of Behavioural Medicine (ICBM) and meet with Dr Sabin, an expert in child obesity and Director of Endocrinology, Diabetes and Obesity at the Royal Children's Hospital, Melbourne, Australia, 6 – 11 December 2016.

Dr Karolina Stasiak
Dept. of Psychological Medicine, University of Auckland

To chair a symposium at the International Society for Research on Internet Interventions (ISRII) 8th Scientific Meeting entitled "Tales from the coalface: Delivering child and adolescent anxiety and depression e-therapies at a community and national level", Seattle, USA, 7 – 9 April 2016.

Dr Francisco Javier Virues-Ortega
School of Psychology, University of Auckland

To participate as a leading scientist in the II European Association of Behaviour Analysis Summer Seminar, Cadiz, Spain, 5 – 8 July 2017.

Dr Grace Wang
Department of Psychology, Auckland University of Technology

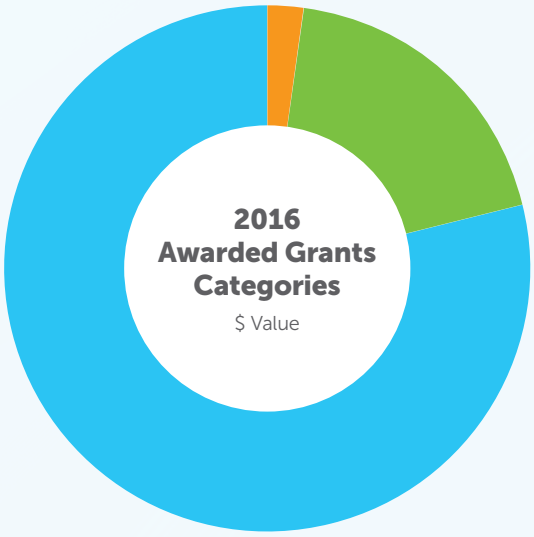
To attend the International Pharmco-EEG Society (IPEG) meeting, Nijmegen, The Netherlands, and a laboratory visit to Nottingham Trent University, Nottingham, UK, 26 – 31 October 2016.

Dr Siouxsie Wiles
Dept. of Molecular Medicine & Pathology, University of Auckland

To attend the Colorado Mycobacteria meeting, Colorado, USA, 7 – 20 June 2016.

GRANTS COMPLETED

58 Grants Awarded Totalling $3,626,944



Population Health and Community (6)	$82,190	2%
Clinical (12)	$691,210	19%
Biomedical (40)	$2,853,544	79%

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

Grants Completed

PROJECTS

WRITTEN EMOTIONAL DISCLOSURE AND SURGERY (1112013)

A/Prof Elizabeth Broadbent, Prof John Windsor, Prof Andrew Hill, A/Prof Roger Booth
Dept of Psychological Medicine,
University of Auckland

Left to Right: Dr Heidi Koschwanez, Dr Elizabeth Broadbent and Hayley Robinson

Prior research has shown that psychological stress can delay wound healing. One kind of psychological intervention to reduce distress is expressive writing, which involves writing emotionally about upsetting events. Expressive writing has been shown to improve the healing of small punch biopsy wounds. This randomized trial aimed to investigate whether expressive writing prior to surgery could both reduce stress and improve surgical wound healing. 76 bariatric surgery participants were recruited and were randomized to either write about a neutral topic (daily activities) or expressive writing. Results showed that contrary to our hypothesis, people writing about daily activities healed significantly better than those who wrote about emotional life events. Further analysis showed that the more people wrote about activities related to the surgery (such as packing an overnight bag), the better they healed. Many patients in the expressive writing group wrote about how anxious they were prior to surgery. This suggests that making concrete plans prior to surgery may be better for reducing stress and improving healing than writing about your emotions. Future research could investigate whether a specifically designed pre-surgical planning intervention can reduce surgical anxiety and improve wound healing.

TARGETING REPLICATION OF A HUMAN RESPIRATORY VIRUS (1113003)

Dr Esther Bulloch, Dr Richard Kingston
School of Biological Sciences,
University of Auckland

Left to Right: Dr Richard Kingston, Nicole Herr and Dr Esther Bulloch

Respiratory viruses are a major cause of hospitalization of infants and immune-compromised individuals. The long-term goal of our research is to develop antivirals against the paramyxoviruses, a family of viruses that includes mumps virus, respiratory syncytial virus and the human parainfluenza viruses. Vaccines are only available against some paramyxoviruses and there are no effective therapeutics to treat infection. Paramyxoviruses replicate in human cells using a complex protein called the RNA polymerase. This protein consists of at least four different functional units (enzymes) fused together and it is difficult to study in its entirety. Our strategy is to divide the RNA polymerase into its individual functional units for molecular studies. In this AMRF-funded project we focused on the RNA polymerase from mumps virus and a poorly studied human parainfluenza virus (HPIV4b). We used a technology called Domain Seeking to map the boundaries between the different functional units of the RNA polymerases from these viruses. Based on the Domain Seeking results we then designed and produced a series of fragments of the RNA polymerase. We are now testing these to determine which encompass intact functional units and are suitable for further study. In the future we will investigate each of these functional units to better understand how paramyxoviruses replicate and to design potential antivirals to treat infection.

REGULATION OF CREATINE SYSTEM IN NEURONS (1113024)

A/Prof David Christie, A/Prof Nigel Birch, Ms Joanna Dodd
School of Biological Sciences,
University of Auckland

Joanna Dodd and Associate Professor David Christie

The survival and normal function of neurons in the brain relies on the supply of energy. Much of this is produced by mitochondria, organelles that act as the power house of the cell. Many neurodegenerative diseases share an energy deficit as a common feature, so we investigated agents/ treatments with the potential to protect neurons by promoting mitochondrial function. Creatine, a well-known dietary supplement, is one such molecule. To be effective creatine must either be synthesized within, or taken up by neurons, and also converted to phosphocreatine. These processes require a group of 'creatine system' proteins. We used cultured rat neurons as a model to investigate how the levels of these proteins are regulated as neurons develop and differentiate. We cultured neurons as they develop for up to 21 days using three different conditions: normal culture (Nb) medium; Nb medium containing creatine; and, a new commercial medium (NbActiv4) that enhances synaptic activity and connections while differing from standard medium only by the presence of oestrogen, creatine and cholesterol. Protein and RNA extracts were prepared from cells cultured for the various times and conditions. The expression of specific proteins and genes were studied by western blotting and quantitative PCR, respectively. We have identified that the protein and RNA levels for the transporter

required for creatine uptake, and AGAT (a key enzyme required for creatine synthesis), increase with development and are reduced by media that contain creatine. It is apparent that creatine taken up by neurons regulates creatine synthesis and uptake. The project has extended our knowledge of the regulation of creatine system proteins known to be important to maintain the energy required for neuronal function and survival.

DEVELOPMENT OF MULTI-MODAL ANTIMALARIAL DRUG CONJUGATES (1113004)

A/Prof Brent Copp, Dr Norrie Pearce
School of Chemical Sciences,
University of Auckland

Associate Professor Brent Copp and Dr A. Norrie Pearce

Despite a massive international collaboration and significant progress being made to reduce the number of infections, malaria continues to exert a devastating toll upon the populations of some of the world's poorest countries. Many antimalarial drugs have lost their efficacy due to drug resistance and alarmingly, resistance to the most effective drug in the antimalarial arsenal, artemisinin, has recently been detected in the Thailand and Cambodia area. We have used medicinal chemistry to create new molecules that combine the antimalarial activities of three different classes of drugs – polyamines, trioxolanes and primaquine. We have demonstrated that these new multi-modal drugs are exceptionally active towards a drug-resistant strain of Plasmodium falciparum, but did not match the levels of activity exhibited by artesunate-derived drugs in in vivo testing. We are continuing to develop these multi-modal antimalarials, focusing on drugs that combine the potent activities of artesunate and primaquine in the same molecule. It is anticipated that such multi-modal drugs will help circumvent antimalarial drug resistance.

STUDIES OF THE EARLIEST EVENTS OF ALZHEIMER'S DISEASE IN THE ADULT HUMAN BRAIN (1113025)

A/Prof Maurice Curtis, Prof Richard Faull
Centre for Brain Research,
University of Auckland

Associate Professor Maurice Curtis and Sir Richard Faull

The origin of abnormal proteins that accumulate in Alzheimer's disease are thought to arise in the olfactory bulb where smell is encoded in the brain. Our studies are aimed at tracking the changes that occur in the human olfactory bulb for the first time with a mind set to create a 3D computed model of the olfactory system to allow the relationship of the key anatomical structures to be visualised in proximity to the pathological proteins. Our work demonstrates the first version of this 3D olfactory bulb, which reveals alterations in the size of the functional units in Alzheimer's disease. Furthermore we performed a detailed neuron spine analysis in the hippocampus, which is the area that degenerates in Alzheimer's disease causing memory loss. Unfortunately our results to date have had limited relevance due to the marked variability between brains used.

FUNDED BY: W & WAR Fraser Charitable Trust

URATE: AN IMPORTANT MEDIATOR OF BONE TURNOVER? (1113015)

Prof Nicola Dalbeth, Dr Jacquie Harper, Prof Jillian Cornish
Dept of Medicine, University of Auckland

Professor Nicola Dalbeth

Elevated urate levels in the blood are present in approximately 20% of the adult population. Recent observational studies have reported that high urate levels are protective in developing thin bones (osteoporosis) and fractures. This laboratory study aimed to understand how urate interacts with bone cells. We studied the effects of urate on bone cells involved in maintaining the structure of health bone (osteoclasts, osteoblasts and osteocytes). Our research has shown no evidence that urate directly interacts with bone cells to increase bone density. This project has provided important new information about the biological role of urate on bone turnover. Specifically, our laboratory data do not support the concept that urate has a direct anabolic effect on bone. These results have important implications for patients on therapies that reduce serum urate concentrations.

Grants Completed continued

EXTRACELLULAR MATRIX MECHANISMS OF MYELINATION FAILURE FOLLOWING PRETERM BRAIN ISCHEMIA (1113021)

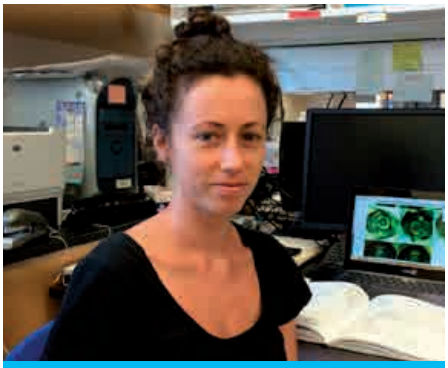
Dr Justin Dean
Dept of Physiology, University of Auckland

Dr Justin Dean

The white matter regions of the brain are important for transferring signals between different brain structures. For rapid movement of these brain signals, cells in the white matter called oligodendrocytes produce an insulating material called myelin. In preterm born babies, oligodendrocytes show a particular vulnerability to injury resulting from low brain blood flow, leading to loss of myelin and cerebral palsy, a devastating lifelong movement disorder for which there is no cure. Therefore, there is a need for new therapies. In humans, although oligodendrocytes are easily killed, we now know that they rapidly grow back. Strikingly, for unknown reasons these new oligodendrocytes fail to properly mature, and do not produce myelin, in areas of injury. In this study we have found that a molecule called hyaluronan is highly join upregulated preterm ischemic white matter injury, and that hyaluronan is degraded by an enzyme in the brain called PH20. These "fragments" of hyaluronan can act on oligodendrocytes to stop them maturing correctly to make myelin. Further, treatment with the novel PH20 inhibitor, Subr3, was found to stop the degradation of hyaluronan, and promote oligodendrocyte myelination. Thus, targeting hyaluronan signalling with SuBr3 may be a novel treatment strategy to promote normal white matter development following preterm brain injury.

ROLES FOR CATION CHLORIDE COTRANSPORTERS IN DIABETIC CATARACT (1113006)

Professor Paul Donaldson,
Dr Irene Vorontsova
School of Medical Sciences,
University of Auckland



Dr Irene Vorontsova in her new lab at University of California Irvine where she is learning to use the zebra fish as a model system to study eye diseases.

We have shown that dysfunction in the ability of lens to regulate its volume is an underlying cause of diabetic lens cataract. We have identified the key membrane transport proteins that effect changes in lens volume. A PhD student, Irene Vorontsova initially used her AMRF Senior Scholarship to identify the regulatory pathway that modulates transporter activity. This current grant allowed Dr Vorontsova to test the functionality of this pathway before taking up a postdoctoral position in the USA. MSc student Chiharu Wickremesinghe has built on Irene's work and will determine how these pathways are disrupted in the diabetic lens.

FUNDED BY: The Hugh Green Fund

GENDER INFLUENCES ON SOCIAL MODELLING OF MEDICATION EFFECTS (1115020)

Dr Kate Faasse
Psychological Medicine,
University of Auckland

Dr Kate Faasse

This research project aimed to investigate the influence of the social modelling of treatment side effects and treatment benefits (compared to no modelling) on placebo treatment effectiveness and symptoms. In addition, this study aimed to investigate the role of both participant and model gender, and participant empathy, in response to social modelling. Data collection for this project (N = 144 participants) was completed in the first half of 2016 and data analysis has been completed. We found that social modelling of symptoms can increase reported side effects following placebo treatment, and this effect appears to generalise to a broader range of symptoms over time. Female participants experience a broader range of symptoms following placebo treatment than their male counterparts. Participants higher in empathy showed stronger responses to social modelling, but this effect was limited to symptoms reported soon after modelling and did not hold at 24-hour follow-up. The write-up of the results of the study has almost been completed and will be submitted to a peer reviewed journal for consideration shortly.

FUNDED BY: Donation from Sanford Limited

REDUCING FGF23 IN CHRONIC KIDNEY DISEASE (3113014)

Dr Christopher Hood, Dr Mark Marshall, Dr Joanna Dunlop
Renal Department, Middlemore Hospital, Counties Manukau District Health Board

Dr Christopher Hood

Chronic Kidney Disease (CKD) is a common condition which is associated with heart failure and cardiac death. Recent work has identified the hormone FGF23 as a likely cause of the heart failure seen in CKD patients. A number of international teams have been investigating treatments that might reduce FGF23 levels in CKD patients, so far with limited success. Niacinamide, the first metabolic by-product of vitamin B3 has many characteristics suggesting it should be an excellent method of reducing FGF23 levels and thus reducing cardiac disease in patients with CKD.

With funding from the AMRF, we successfully completed the world's first trial investigating oral Niacinamide as a treatment aimed at reducing FGF23. This trial involved 90 patients who took the study medications for a period of 4 months each. Results are now available for analysis and will produce an important, statistically powerful answer to this important research question. These results will be published in international journals and shared with other teams aiming to reduce cardiac disease in CKD.

MAINTAINING REDOX BALANCE IN THE AGEING EYE (1115008)

Dr Julie Lim, Dr Joanna Black, Prof Paul Donaldson
Dept of Optometry & Vision Science, University of Auckland

Front to Back: Renita Martis (PhD student), Dr Julie Lim and Professor Paul Donaldson

With advancing age, oxidative stress results in redox imbalance and eye diseases which threaten the sight of the elderly. Recent work from our laboratory has confirmed a role of CGAP in maintaining cysteine/cystine redox balance. In knockout mouse where xCT the subunit of CGAP responsible for transporter function is removed, the absence of xCT results in significantly higher plasma cystine concentrations relative to cysteine, reminiscent of that observed in older mice. This indicates that ageing is accelerated in these knockout mice. Eye examinations revealed age-related pathologies in the lens and retina of the knockout mouse only. Measurements of the antioxidant glutathione (GSH) showed that xCT appears to be important for GSH synthesis in the retina, but not the lens. This suggests that different mechanisms are responsible for the pathology observed in the lens. Collectively, these findings demonstrate the xCT KO mouse to be an excellent model to study age-related eye diseases and in identifying underlying pathways that contribute to pathologies in the aging eye. This study will be used to inform future work in providing essential information for the design of effective therapies to delay the onset of age-related eye diseases.

FUNDED BY: AC Horton Estate

EFFECTS OF PARKINSONIAN TOXINS ON THE LOCUS COERULEUS: IMPLICATIONS FOR UNDERSTANDING NON-MOTOR SYMPTOMS OF PARKINSON'S DISEASE (1113007)

Prof Janusz Lipski, Dr Andrew Yee, Dr Peter Freestone, Dr Ji-Zhong Bai
Dept of Physiology, University of Auckland

Left to Right: Professor Janusz Lipski, Dr Peter Freestone and Dr Andrew Yee

Parkinson's disease (PD) is a relatively common degenerative brain disorders leading to slowness of movement, tremor in hands and muscle stiffness. Importantly, PD patients also suffer from debilitating non-motor symptoms, such as sleep disturbance, cognitive and mood disorders and dysfunction of the cardiovascular system, bowel and bladder, which severely impact the quality of life of those affected by the disease. Previous research indicated that at least some of these non-motor symptoms are due to degeneration of nerve cells in the Locus Coeruleus (LC), but the mechanism of this damage was unknown. Remarkably, degeneration of the LC can exceed damage of the Substantia Nigra (SN) associated with the 'classical' motor symptoms of the disease. Our study, conducted on isolated animal brain tissue, looked at the effects on LC and SN neurons of two PD-related environmental toxins: rotenone and MPP+. We have demonstrated that despite being damaged earlier in the progression of PD, in our model LC neurons are less affected by these toxins than SN neurons. This research advanced our understanding of the mechanisms of action of parkinsonian toxins on neurons vulnerable in PD, and sheds new light on the complex relationship between the motor and non-motor symptoms in this debilitating disorder

FUNDED BY: Angus Family Trust

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Grants Completed continued

TECHNOLOGY ASSISTED EXERCISE-BASED CARDIAC REHABILITATION (1113020)

Prof Ralph Maddison, Dr Robyn Whittaker, Dr Anna Rolleston, Hon. Prof Ralph Stewart, Dr Nicholas Gant, Dr Ian Warren, Dr Jonathan Rawstorn
National Institute for Health Innovation, School of Population Health, University of Auckland

Left to Right: Jonathan Rawstorn (PhD student), Professor Ralph Maddison and Dr Nick Grant

Exercise is essential to aid recovery from a heart attack. In this study we compared the effectiveness of home-based monitored exercise using mobile phones and monitoring technology (called REMOTE) to existing supervised exercise cardiac rehabilitation. The REMOTE platform for delivering the exercise programme has been tested and is working well, with positive feedback from participants. We recruited 162 participants and allocated these at random to either 12 weeks of standard supervised exercise cardiac rehabilitation or to the new mobile phone programme (REMOTE). As hypothesised, results show no difference in oxygen uptake, modifiable cardiovascular risk factors, or exercise-related psychological outcomes between conditions. Intervention group participants reported high usability, acceptability, and satisfaction for the technology-assisted programme.

FUNDED BY: AC Horton Estate

A BREATH OF FRESH AIR: MEASURING OXYGEN IN DISEASED KIDNEYS (1113016)

Prof Simon Malpas, Dr Maarten Koeners
Dept of Physiology, University of Auckland

Professor Simon Malpas

Kidney disease is a growing global public health problem. Low tissue oxygen and kidney disease are associated, although the mechanisms responsible and their time course have been ill-defined. This project utilized state-of-the-art techniques to measure the time course of kidney oxygen levels during the development of chronic kidney disease in rats. The findings demonstrated that oxygen levels in the kidney decreased prior to signs of overt kidney disease, suggesting that low kidney oxygenation may be driving disease. In addition, we investigated the role of angiotensin II (ANG II) in mediating the low kidney oxygen and found that ANG II reduced the levels of kidney oxygen by reducing oxygen supply. Together, the results support the hypothesis that low kidney tissue oxygen may be contributing to the development of chronic kidney disease. These pre-clinical findings provide important clues for the understanding and treatment of kidney-related cardiovascular disease in humans.

MELANOCORTIN TREATMENT FOR OBESITY (1112016)

Dr Kathy Mountjoy, Dr Ailsa McGregor
Dept of Physiology, University of Auckland

Dr Kathy Mountjoy and Dr Ailsa McGregor

The melanocortin system is the most important hormonal system known to regulate mammalian body weight. To date, no successful anti-obesity therapies have been developed to target this system because we do not understand which natural melanocortin hormones are responsible for body weight regulation. ą-Melanocyte stimulating hormone (ą-MSH) is assumed worldwide to be the natural melanocortin hormone that regulates food intake and body weight and it is generally believed that mimicking ą-MSH would be a successful anti-obesity treatment. Our data shows that there is a second naturally occurring melanocortin peptide hormone, desacetyl-ą-MSH, which is equally effective at reversing mouse obesity. In the absence of both ą-MSH and desacetyl-ą-MSH male and female mice develop high-fat diet-induced severe obesity. Administration of either peptide hormone into mouse brain reverses this obesity, even while the mice continue to eat a high-fat diet. We show that the MSH peptides regulate body weight by altering food intake and energy expenditure and the mechanisms used by these peptide hormones differ between male and female mice. Future studies that address the different functions for ą-MSH and desacetyl-ą-MSH in male and female mouse body weight may advance understanding about the higher prevalence for obesity in females worldwide and could lead to effective prevention or therapies for both male and female obesity.

REVERSAL OF MULTI-DRUG RESISTANCE BY DRUG-PHYTOCHEMICAL COMBINATION THERAPY (1113026)

A/Prof James Paxton, Dr Zimei Wu, Dr Yan Li
Dept of Pharmacology & Clinical Pharmacology, University of Auckland

A major factor responsible for the failure of cancer chemotherapy is the development of multi-drug resistance due to upregulation of efflux pumps which can efficiently remove the drug from the cancer cell, thus causing it to lose its effect. We have developed a novel nano-vesicle (a liposome) which can concurrently deliver to the tumour, both the anti-cancer drug plus a natural dietary compound, curcumin, which we have identified as a potent inhibitor of these efflux pumps. These combination liposomes exhibited considerably greater anti-tumour efficacy against resistant pancreatic cancer cells due to greater intra-cellular drug accumulation. However, while optimising the curcumin/drug combination ratio, we observed that, with increasing curcumin concentrations relative to the drug, the combination surprisingly became less effective, with the cancer cells becoming more resistant. Further investigations revealed that curcumin was also an inhibitor of specialised transporters necessary for the uptake of some anticancer drugs into the cancer cell. This is the first report of a dietary compound, such as curcumin, with the ability to inhibit these specific cellular uptake transporters. Our results suggest caution with the clinical testing of such combinations due to the possibility that curcumin and similarly structured analogues may inhibit the entry of active drug into the target cells.

METFORMIN IN GESTATIONAL DIABETES: THE OFFSPRING FOLLOW UP AT 7-9 YEARS (2111013)

Dr Janet Rowan, Prof Elaine Rush, Dr Jun Lu, Dr Malcolm Battin, A/Prof Lindsay Plank
National Womens Health, Auckland District Health Board

Professor Elaine Rush and Dr Janet Rowan

We previously performed a randomized trial from 2002-2006 comparing metformin tablets with insulin injections to treat women who had diabetes during pregnancy (gestational diabetes). The original trial showed that metformin was a safe and effective alternative to insulin with respect to pregnancy outcomes. Metformin crosses the placenta, so we have been following the children to see if there are any long term effects particularly relating to measurements of body fat and how the body handles sugar. At two years of age, body fat percent was no different between children whose mothers had been treated with insulin or metformin. In study we have just completed, we measured 99 children between 7-9 years of age. Preliminary analysis shows that there were no significant differences in body fat percent, abdominal fat percent or glucose tolerance between children whose mothers had been randomised to metformin compared with insulin. We hope to plan further follow up when the children are approximately 15 years of age.

FUNDED BY: Marion Ross Memorial Fund

SELECTIVE INHIBITORS OF MRSA PYRUVATE KINASE AS STRUCTURALLY UNIQUE, NEXT-GENERATION ANTIBIOTICS (1114007)

Dr Jonathan Sperry
School of Chemical Sciences, University of Auckland

Dr Jonathan Sperry

In this two-year collaborative project we synthesised several compounds for an evaluation of their inhibitory properties against MRSA pyruvate kinase (PK), a "hub" protein that represents a novel target for antibiotic development. It was discovered that the presence of the O-heterocycle results in complete loss of selectivity over human isoforms of the enzyme, and that the first class of inhibitors were relatively poor antibiotics, likely due to poor cellular penetration. Focus switched to the synthesis and biological evaluation of more drug-like natural product candidates, along with those that are locked in a rigid conformation that mimics the natural product leads described by our collaborators, the results of which are eagerly awaited. Although this project has not resulted in a candidate that exhibits antibiotic activity in vivo, we have made some good progress towards narrowing down the key pharmacophore required for inhibition of MRSA PK, the results of which will contribute to the design of better inhibitors as the collaboration continues. This funding has allowed us to establish an ongoing collaboration with world class biologists in Canada and helped establish a thriving antibacterial research programme; all those involved in the project are deeply grateful for this support.

Grants Completed continued

IMPROVING TEAM COLLABORATION IN THE OPERATING THEATRE (1112014)

A/Prof Jennifer Weller, Prof Alan Merry, Prof Ian Civil, Ms Wendy Guthrie, Dr Craig Webster, Dr Jane Torrie, Dr Andrew MacCormick, Dr David Cumin, Dr Matt Boyd
Centre for Medical and Health Sciences Education, University of Auckland

Associate Professor Jennifer Weller

Failures in communication and teamwork in the operating room lead to patient harm. The Multidisciplinary Operating Room Simulation (MORSim) project was designed to be a course for teams of operating room staff to train together and improve teamwork. The course consisted of three simulated surgical cases with debriefs and lectures. A special effects company helped to make the simulations realistic and the course was administered at the University of Auckland Simulation Centre for Patient Safety. A total of 20 course days were run with 120 staff, including surgeons, anaesthetists, and nurses. The vast majority (98%) of participants said the training day was useful and almost 90% said they would change their practice as a result. There was a significant improvement in communication and information sharing over the course day and improved teamwork behaviours were also observed in the clinical environment. Following this successful pilot, the Accident Compensation Commission have funded the MORSim course to be rolled-out nationally in all 20 District Health Boards in New Zealand. The project has been awarded $4,800,000 for the first two and a half years.

HOMING IN ON THE EPITOPE TARGETS FOR COGNITIVE-ENHANCING AND PROTECTIVE NR1 ANTIBODIES (1113009)

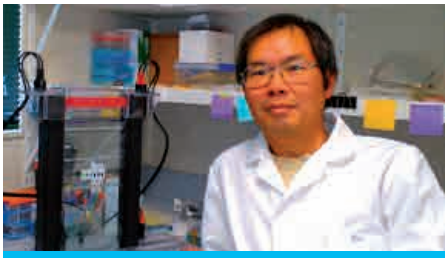
A/Prof Deborah Young
Dept of Pharmacology & Clinical Pharmacology, University of Auckland

Associate Professor Deborah Young (standing directly left of CBR logo) and her research team.

The project aim is to understand why antibodies to the NR1 subunit of NMDA receptors (NR1 antibodies) can enhance learning and memory in animal models, but on the other hand, produce detrimental effects such as rapid memory loss and seizures as observed in NMDA receptor encephalitis patients. Our exciting results suggest that the contrasting effects are caused by NR1 antibodies binding to different places on the NR1 subunit, resulting in altered function of the NMDA receptor. The beneficial NR1 antibodies increase the numbers of NMDA receptors at the synapse, the point of communication between neurons, whereas the detrimental NR1 antibodies impair signalling between neurons. The outcomes of this project have led to the identification of a drug target that will contribute to the development of a new class of drugs suitable for enhancing learning and memory function.

TARGETING THE MECHANISM OF HOST RECOGNITION TO PREVENT BACTERIAL INFECTIONS (4114009)

Dr Xue-Xian Zhang, A/Prof John Harrison, Dist. Prof Paul Rainey, Dr Stephen Ritchie
Institute of Natural and Mathematical Sciences (INMS), Massey University at Albany, Auckland



Dr Xue-Xian Zhang

This project addresses a crucial gap in our current understanding of how bacteria cause disease - namely, how pathogenic bacteria recognize vulnerable hosts for successful colonization and immune evasion. Specifically, we test a new hypothesis that the nosocomial pathogens recognize histidine and its derivative urocanate in human tissues and use them as a trigger for bacterial invasion. The major task of this AMRF-funded pilot study is to develop the analytic techniques required for detection of histidine and urocanate in chemically complex human tissue samples, including a preliminary screening of ~200 human specimens. With the help of Dr Simon Liu who had worked part-time in this project, we have successfully developed both the chemical HPLC methods and biosensors for measuring histidine and urocanate concentrations in human tissue samples. A total of 191 humans specimen (sputum, urine and wound fluid) were collected (and analysed) from patients at the Auckland City Hospital. The data revealed some significant findings such as a positive correlation between histidine and urocanate, and significant effects of tissue type on urocanate. Together, these results have laid a good foundation for further investigations into the association between histidine or urocanate concentration and predisposition to bacterial infection.

POSTDOCTORAL FELLOWSHIPS

MATERNAL DIET INDUCED PROGRAMMING OF OFFSPRING IMMUNE FUNCTION (1313003 & 1714002)

Dr Clare Reynolds
Liggins Institute, University of Auckland

Dr Clare Reynolds

Unbalanced maternal diet, whether under nutrition or over nutrition, predisposes offspring to adult obesity, type-2 diabetes and cardiovascular disease. These conditions are intrinsically linked with low-grade inflammation. While evidence of immune cell infiltration and increased expression of inflammatory mediators have provided many clues as to the mechanisms through which "meta-inflammation" instigates metabolic dysfunction, there are many questions which remain unanswered, particularly in relation to the developmental programming of health and disease. This study investigated diet-induced inflammation during pregnancy and subsequent long-term offspring metabolic disease in an established rat model of developmental programming. We assessed the origins of inflammation in mothers and offspring by characterizing inflammatory readouts in the placenta, bone marrow and metabolic organs (adipose tissue and liver). We also investigated glucose tolerance, body composition, pubertal onset (males and females) and oestrus cycle dysfunction. This research demonstrated that high-fat diet consumption during pregnancy predisposed to increased risk of obesity and metabolic dysfunction. Furthermore we determined, by supplementing maternal diets with the anti-inflammatory lipid CLA, that maternal diet-induced developmental programming can be reversed by nutritional strategies. This project allowed us to establish the importance of inflammation in developmental programming and potentially develop therapeutic anti-inflammatory strategies.

FUNDED BY: David and Cassie Anderson Medical Trust

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DOCTORAL SCHOLARSHIPS

GLUTAMATE RECEPTORS IN HUMAN MELANOMA (1211001)

Stacey D'mello
Dept of Molecular Medicine & Pathology, University of Auckland

Stacey D'mello

The aim of this project was to determine whether glutamate signalling acting through the N-methyl-D-aspartate receptor (NMDAR) contributes to the biology of human melanoma. We found that mutations in one of the NMDAR subunits, called GRIN2A, were present in four of 20 cell lines derived from patients with metastatic melanoma. The presence of these mutations correlated with faster disease progression and shorter overall survival of patients in this cohort. We confirmed that various NMDAR transcripts were present in all cell lines and that some proteins were expressed. NMDAR inhibitors caused variable levels of inhibition of melanoma cell proliferation and invasion in vitro. We detected calcium ion fluxes through the NMDAR in melanoma cells. Melanoma cells themselves released glutamate into media, which may further modulate cancer cell biology. We suggest that aggressive melanomas release glutamate to gain a survival advantage but they also adapt and escape glutamate-mediated toxicity by down-regulating NMDAR expression and accumulating mutations in the NMDAR-encoding genes. We propose that GRIN2A can act as an oncogene or a tumour suppressor, depending on glutamate levels in the tumour.

FUNDED BY: John Jarrett Trust

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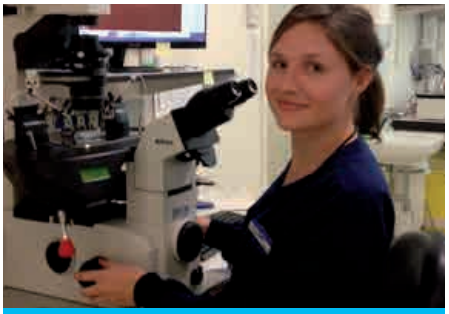
AN INVESTIGATION OF BIOMARKERS FOR IMPROVED EMBRYO SELECTION IN IVF (1212001)

Elizabeth Hammond
Dept of Obstetrics & Gynaecology, University of Auckland



Elizabeth Hammond

Around one in six couples will experience infertility and may need to use in vitro fertilisation (IVF) to have a family. During IVF, multiple embryos are grown in liquid droplets in a laboratory and checked daily to determine whether they are developing normally. Three to five days after fertilisation, a single embryo is transferred into the uterus, but currently only one in four results in a successful pregnancy. This is because the use of morphology to select an embryo for transfer has a poor ability to determine viability. The current study investigated non-invasive biomarkers of embryo viability to address this. The first aim was to investigate the genetics of eggs

Grants Completed continued

in a novel bovine model of human IVF. It was found that the mitochondrial DNA, which is involved in energy production, may be susceptible to damage after ageing. The second aim investigated the novel strategy of using two non-invasive biomarkers of embryo viability in parallel. In human embryos, the cumulus cells which surround the egg were used in conjunction with a time-lapse microscope, which enabled embryo development to be monitored every 5 minutes, instead of once daily. These two biomarkers showed correlation with each other and with embryo viability. The third aim was to investigate genetic material which is released into the liquid droplet that the embryo grows in. This was characterised to assess its potential to be a novel biomarkers of embryo viability. Ultimately, this study aimed to assess the potential clinical benefit of biomarkers for improved IVF success.

FUNDED BY: John Jarrett Trust

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THE EFFECT OF NEONATAL HYPOGLYCAEMIA ON VISUAL DEVELOPMENT (1212002)

Nabin Paudel
School of Optometry & Vision Science, University of Auckland

Nabin Paudel

The main aim of this research project was to explore the effect of low blood sugar concentrations after birth on the subsequent development of vision. We demonstrated that the current treatment regimen for neonatal hypoglycaemia ie, maintaining blood glucose at a concentration above 2.6 mmol/L allows for normal development of binocular visual acuity (the ability to see distant object clearly with both eyes open), stereopsis (3D perception) and global motion perception (the ability to perceive complex motion). Furthermore, we found that visual status obtained with established clinical vision tests for 2-year-old children were not prognostic of visual outcome at 4.5 years of age.

OTHER GRANTS

SIR HARCOURT CAUGHEY AWARD

TO COMPLETE A YEAR AS A CLINICAL AND RESEARCH FELLOW WITHIN THE GYNAECOLOGICAL ONCOLOGY TRANSLATIONAL UNIT OF THE INSITUT GUSTAVE ROUSSY, AN INTEGRATED CANCER CENTRE OF EXCELLENCE IN FRANCE (2514006)

Dr Soizick Mesnage
Medical Oncology, Auckland District Health Board

Dr Soizick Mesnage

The AMRF Sir Harcourt Caughey Award has allowed me to complete a year as a clinical and research fellow within the Gynaecological Oncology Translational Unit of the Insitut Gustave Roussy, an integrated cancer centre of excellence in France. During this fellowship year my knowledge and experience in the management of patients with gynaecological malignancies, has been expanded to include standard of care at an internationally recognized institute with a wide range of publically funded treatments. My research work has been exceedingly interesting and exciting, the main focus being a translational study of ovarian cancer studying the evolution with chemotherapy of biological features such as immune infiltration, DNA repair capacity and genomic profile of the tumour. This fellowship has been extremely rewarding and contributed positively to my professional development as a medical oncologist with an interest in cancer research. I believe the research I am doing will benefit my future clinical practice of oncology in this era of molecular and personalized cancer care, and allow me to have the knowledge, skills, and experience to contribute to translational research in cancer medicine on my return to New Zealand.

GAVIN AND ANN KELLAWAY MEDICAL RESEARCH FELLOWSHIP

FELLOWSHIP IN THE LABORATORY OF DR GIOVANNI MARSICANO, NEUROSCIENCE MAGENDE, INSERM INSTITUTE, BORDEAUX, FRANCE (1514007)

Prof Michelle Glass
Dept of Pharmacology, University of Auckland

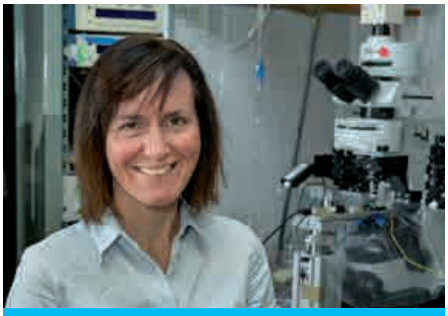
Professor Michelle Glass enjoying a well-earned family day out at Dune du Pilat, during her fellowship at the Inserm Institute, Bordeaux, France

This Fellowship enabled me to attend several conferences/workshops and a University as an invited speaker or participant throughout Europe; the European Workshop on Cannabinoids and the International Cannabis as Medicine Society meeting, Italy; the Spanish

Endocannabinoid Research Society Annual Meeting; the Swiss Endocannabinoid society meeting; the British Pharmacology Society meeting; and the University of Mainz, Germany. These meetings were notable for the extremely high quality of the science that was being presented and the open, honest and respectful way that the invitees discussed the findings in a field where there are many differing opinions. In Bordeaux I joined the laboratory of Dr Marsicano where I worked on an interesting collaborative project that aims to use state-of-the-art techniques to understand the role of G-protein coupled receptors in mitochondria, the power houses of a cell. Whilst I was at INSERM, I was also invited to join the group lead by the Institute Director Dr Pier Vincenzo Piazza working on the interaction of a specific steroid with cannabinoid receptors. The outcome of this work is that the group at INSERM have agreed to fund a technician and consumables in my laboratory for the next year to enable us to contribute to the wider project. This is a fantastic outcome for my group as it provides us with an opportunity to join a very high profile study which could well result in development of medications in the future. Being based in Europe and able to use the conferences and my time in INSERM to meet in person with collaborators and potential collaborators makes such a difference and I have no doubt that the ongoing collaboration with INSERM would not have come about had I not been there in person. Personally being based at such a productive institute with extremely talented people was invigorating, and having the opportunity to live in such a beautiful city as Bordeaux was a once-in-a-lifetime experience, and I am so grateful to the AMRF for enabling me to do this.

TO ACCESS NEW AUTISM MOUSE MODELS AND WORLD-CLASS IMAGING FACILITIES AND TO BEGIN A NEW COLLABORATION EXAMINING THE NEURAL BASIS OF CARDIAC ARRHYTHMIAS (1515001)

A/Prof Johanna Montgomery
Dept of Physiology, University of Auckland



Associate Professor Johanna Montgomery

I was hosted for 4.5 months at Charité University, Berlin, Germany, where I worked with Professor Craig Garner to establish a new phase of our successful collaboration addressing the synaptic basis of Autism Spectrum Disorders (ASD). Specifically, the aims of our experiments were to perform both cellular and behavioural experiments to address the role of zinc in regulating synaptic proteins known to be mutated in ASD. Because low levels of zinc are associated with patients with ASD, and because zinc is known to regulate the synaptic protein Shank3, we performed experiments to test the hypothesis that Shank3 is part of a zinc-mediated signalling pathway, and that zinc mismanagement could be at the heart of autism. During this time at Charité University I also learnt super-resolution imaging techniques. I then moved to the University of Leicester to undertake training that would provide the required expertise to establish a new collaboration in Auckland with physiologists and cardiologists examining the neural basis of cardiac arrhythmias (irregular or abnormal heart beat). We have now successfully established this technique in my lab at the University of Auckland, and we will perform electrophysiological characterisation of these clusters of neurons located on the surface of the heart that are thought to initiate arrhythmias.

TO COMPLETE A MASTERS OF APPLIED STATISTICS AT THE UNIVERSITY OF OXFORD (7515002)

Dr Lisa Pilkington
Dept of Chemical Sciences,
University of Auckland

Dr Lisa Pilkington in Oxford during her fellowship.

I was awarded the Gavin and Ann Kellaway Medical Research Fellowship in 2015 to help fund my studies for the degree of MSc in Applied Statistics at the University of Oxford, UK, from September 2015 - September 2016. I wished to undertake this study to learn and develop skills in applied statistics so I could utilise them, in conjunction with my knowledge as a PhD in medicinal chemistry, to direct research in the field of drug discovery. My programme comprised of both taught papers, in which I learnt a diverse and comprehensive range of statistical theory and techniques and a research project in which I utilised and further developed my understanding and usage of these techniques. In my research project I was able to investigate modelling the biological activity of compounds, based on a number of structure-based factors – predicting if a given compound would induce a biological response and thus have the potential to be a drug or drug-lead. Moving forward, I am looking to further develop these models and this research in the hope that they will aid in the field of drug-discovery.

Grants Completed continued

SIR DOUGLAS ROBB MEMORIAL FUND

PARTIAL FUNDING FOR PUBLICATION IN THE JOURNAL "MELANOMA RESEARCH" (1715003)

Dr Hilary Sheppard
School of Biological Sciences,
University of Auckland

Sheppard, H., Feisst, V., Chen. J., Print, C. and Dunbar, R. (2016) AHNAK is down-regulated in melanoma, predicts poor outcome and may be required for the expression of functional E-cadherin. Melanoma Research; 26(2):108-16.

The journal "Melanoma Research" is ranked 19/61 for dermatology related journals and carries an impact factor of 2.219. It is a well-established international journal with a specific focus on melanoma. Within that focus the breadth of subjects it covers is broad including, but not limited to, molecular biology, cellular biology, pathology and advances in the clinic regarding the prevention, diagnosis and treatment of melanoma.

As far as we are aware this is the first research article to correlate the loss of expression of a protein called 'AHNAK' with melanoma and poor patient outcome.

HEALTHEX EMERGING RESEARCHER AWARD

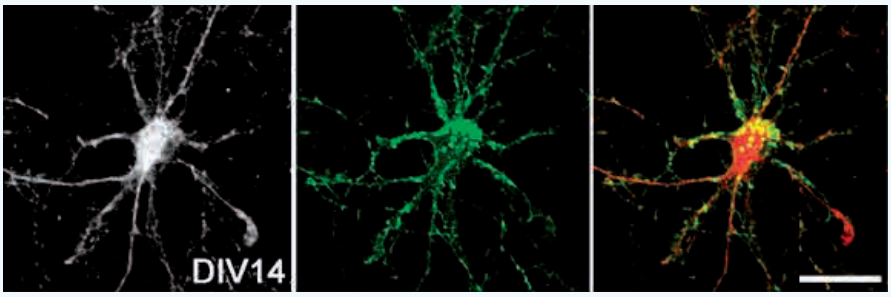
TO ATTEND UNIVERSITAS 21 HEALTH SCIENCES FORUM, PONTIFICIA UNIVERSIDAD CATOLICA, SANTIAGO, CHILE – 21-25 SEPTEMBER 2015, AND TO MEET AND PERFORM EXPERIMENTS WITH HER COLLABORATOR AT THE NEUROSCIENCES CENTRE (6715001)

Miss Lily Chang
Dept of Optometry & Vision Science,
University of Auckland

I would like to thank AMRF for awarding me The AMRF Emerging Researcher Award in 2015. Subsequently, I was able to travel to Chile in September 2015 to present my research at the Universitas 21 (U21) Annual Meeting in Santiago, and to conduct experiments for my PhD project in Valparaiso, Chile. The title of my PhD project is "Molecular and Functional Evidence of Alzheimer's disease (AD) in the Eye: Clinical and Experimental Application", and a natural animal model for AD – the Octondon degus (endemic to Chile) was used for immunohistochemistry of the retina, and in vivo non-invasive examination of their eyes. The clinical ocular assessment of the Octondon degus colony was completed during my time in Valparaiso, Chile, and I was able to proceed with completing my thesis in December 2015. Furthermore, I had the opportunity of presenting my research, exchanging ideas and networking with other researchers from around the world at the U21 Annual Meeting in Santiago. This wonderful experience would not have been possible without the support of AMRF.

FUNDED BY: Wellington Sisters Charitable Trust

PUBLICATIONS



HAS2 PROTEIN EXPRESSION ON CORTICAL NEURONS IN VITRO - Hyaluronan is a sugar that provides strength, lubrication and hydration in the space (known as the extracellular space) around many cells in the body. However, whether neurons in the brain can make their own hyaluronan was unknown.

This image shows neurons from the cortex of the brain grown in culture for 14 days and labelled with a marker for an enzyme responsible for hyaluronan synthesis (HAS2, shown in red) to identify where this enzyme is localised on the neuron. It is also labelled with a cytoskeleton marker (green) to show the structure of the neuron. Scale bar: 30µm.

The data from this study suggests that neurons have the capacity to independently synthesise hyaluronan on multiple neuronal structures throughout their development.

In publication: Fowke T, Karunasinghe R, Bai J, Jordan S, Gunn, A, Dean, J. (2017). Hyaluronan synthesis by developing cortical neurons in vitro. Scientific Reports 7:44135.

Publications

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AMRF AUDITORIUM

University of Auckland
Faculty of Medical and Health Sciences

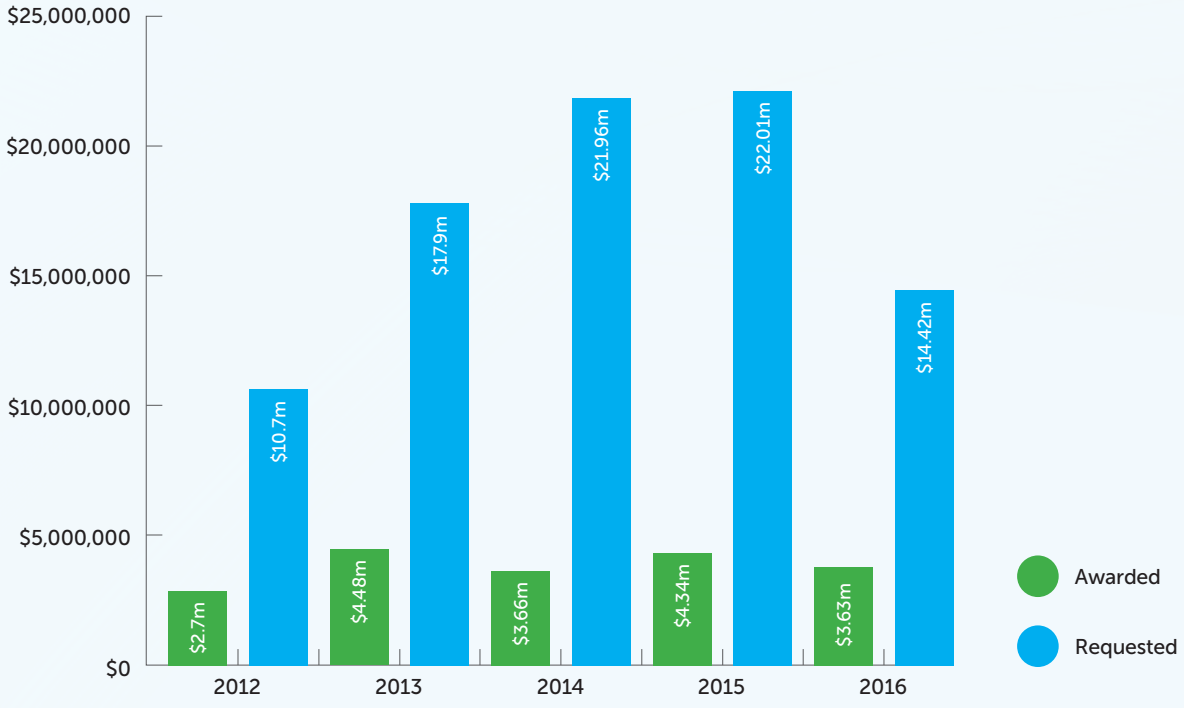
The AMRF Auditorium was made possible through a generous donation from an AMRF benefactor.

AMRF holds two free public lectures each year on topics of interest. See www.medicalresearch.org.nz for past and current lectures.

FINANCIALS 2016

THERE ARE MANY WORTHY REQUESTS FOR FUNDING THAT WE CANNOT SUPPORT.

THANK YOU FOR YOUR GENEROSITY.



FINANCIAL HIGHLIGHTS 2016

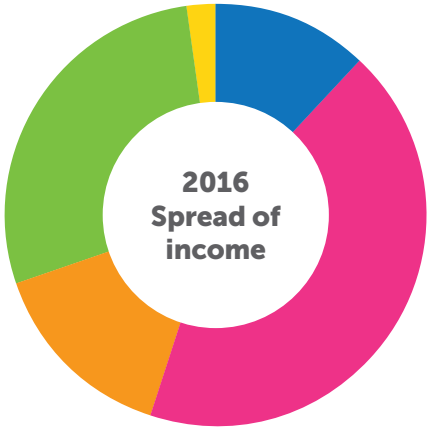
RESEARCH FUNDING 2016 $3.63M **TOTAL RESEARCH FUNDING SINCE 1955 $63.7M**

FINANCIAL PERFORMANCE

	Note	2016 $	2015 $
Income			
Donations / Subscriptions	1	609,608	647,154
Investment Income		2,154,334	2,238,363
Trust Income and External Funding	1	731,277	1,723,452
Legacies/Bequests/Specific Donations	2	1,397,786	1,152,929
Net Gain on realisation of investments		107,698	1,098,027
Net Loss on currency fluctuations		(9,651)	(2,838)
Total		4,991,052	6,857,087

Expenditure					
Operational expenses		395,733		321,005	
(Less Donation)	3	(395,733)	Nil.	(321,005)	Nil.
Research Grants 2016	4		3,322,635		4,080,406
Depreciation on Grant Funded Assets			5,285		4,832
Reduction in value of investments			247,876		419,644
Total			**3,575,796**		**4,504,882**
Net (Deficit) / Surplus			**1,415,256**		**2,352,205**

The summary financial report above has been extracted from the full Audited Financial Statements which can be obtained by contacting the Foundation's office. Tel: 09 9231701 or Email: admin@medicalresearch.org.nz



	2016	2015
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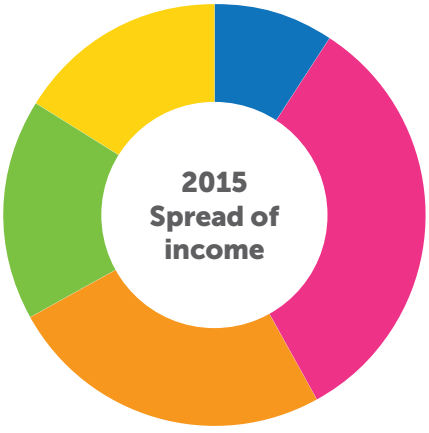

NOTES TO THE 2016 FINANCIAL REPORT

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

Perpetual Guardian Administered Funds	
Barbara Basham Medical Trust	128,000
NR Thompson Charitable Trust	30,000
NH Taylor Charitable Trust	40,000
Room Simmonds Charitable Trust	40,000
J&P Stilson Endowment Trust	100,000
Richardson Trust	307
Rose Richardson Estate	40,000
Edith C Coan Trust	120,000
John A Jarrett Trust	41,783
CE Lawford Estate	3,100

Public Trust Administered Funds	
Acorn Charitable Trust	10,000
Reed Charitable Trust	10,000
Pauline Gapper Charitable Trust	7,500
Audrey Simpson Trust	8,750
Ralph Dingle Trust	3,000
Wellington Sisters Charitable Trust	14,000

Other Trusts/Funds	
Douglas Goodfellow Charitable Trust	195,924
The Kelliher Charitable Trust	60,000
Marion Ross Fund	33,513

2. Legacies, Bequests and Specified Donations 1,397,786

Anonymous

Estate of MA Greenall

Estate of Jack Noel Henderson

Douglas Goodfellow Capital Fund

David Christie Capital Fund

3. Operational Expenses

The Foundation is very grateful for the Harry Goodfellow Fund, Hector Goodfellow Fund and TB & WD Goodfellow Fund for the external funding of operational expenses.

4. Research Funding Approved During Year

PROJECT GRANTS GENERAL (23)	2,650,444
POSTDOCTORAL FELLOWSHIPS (1)	
Edith C Coan Research Fellowship	199,473
DOCTORAL SCHOLARSHIPS (4)	
AMRF Doctoral Scholarships (2)	215,000
AMRF Brian De Luen Doctoral Scholarship	111,500
Barbara Basham Doctoral Scholarship	128,000
AMRF TRAVEL GRANTS (24)	59,603
OTHER GRANTS (6)	
Kelliher Charitable Trust Emerging Researcher Start-up Grant (2)	60,000
Douglas Goodfellow Repatriation Fellowship extension	195,924
HealtheX Emerging Research Awards (3)	7,000
Total Grants Committed 2016	3,626,944
Less amounts allocated but not required	(304,309)
TOTAL GRANT FUNDING 2016	**3,322,635**

Members, Sponsors & Supporters 2016

WE ARE MOST GRATEFUL TO ALL THE INDIVIDUALS, TRUSTS AND ORGANISATIONS LISTED BELOW WHO HAVE GIVEN GENEROUS SUPPORT TO THE FOUNDATION DURING THE YEAR.

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Hart, Cliff
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Front: (left to right) Jeff Todd, President of the AMRF and Professor Stuart McCutcheon, Vice-Chancellor.

To mark the Auckland Medical Research Foundation's 60th anniversary and the University of Auckland's Faculty of Medical and Health Sciences 50th anniversary the AMRF will donate, in perpetuity, the income from a ring-fenced, $2.5 million portion of our capital fund to the FMHS's Scholar's Fund to provide the salary for a prestigious 5 year fellowship targeted to future leaders called the AMRF Senior Research Fellowship.

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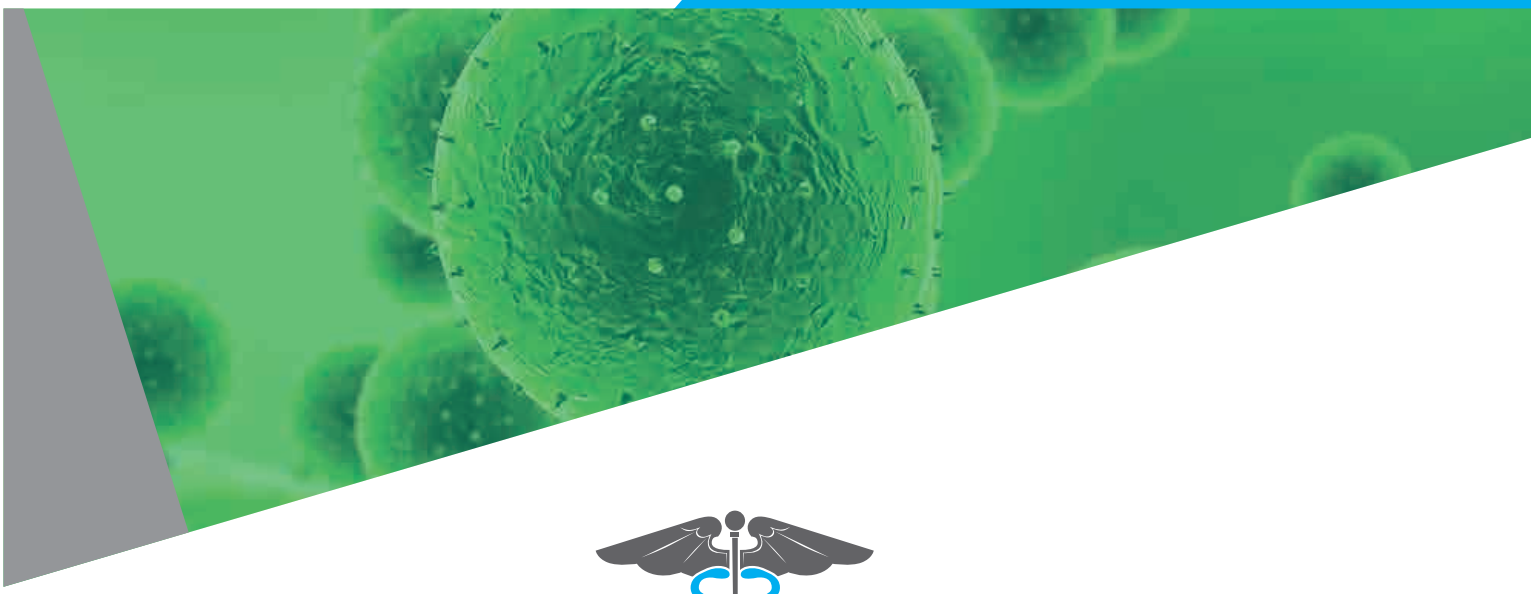

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