Auckland Medical Research Foundation

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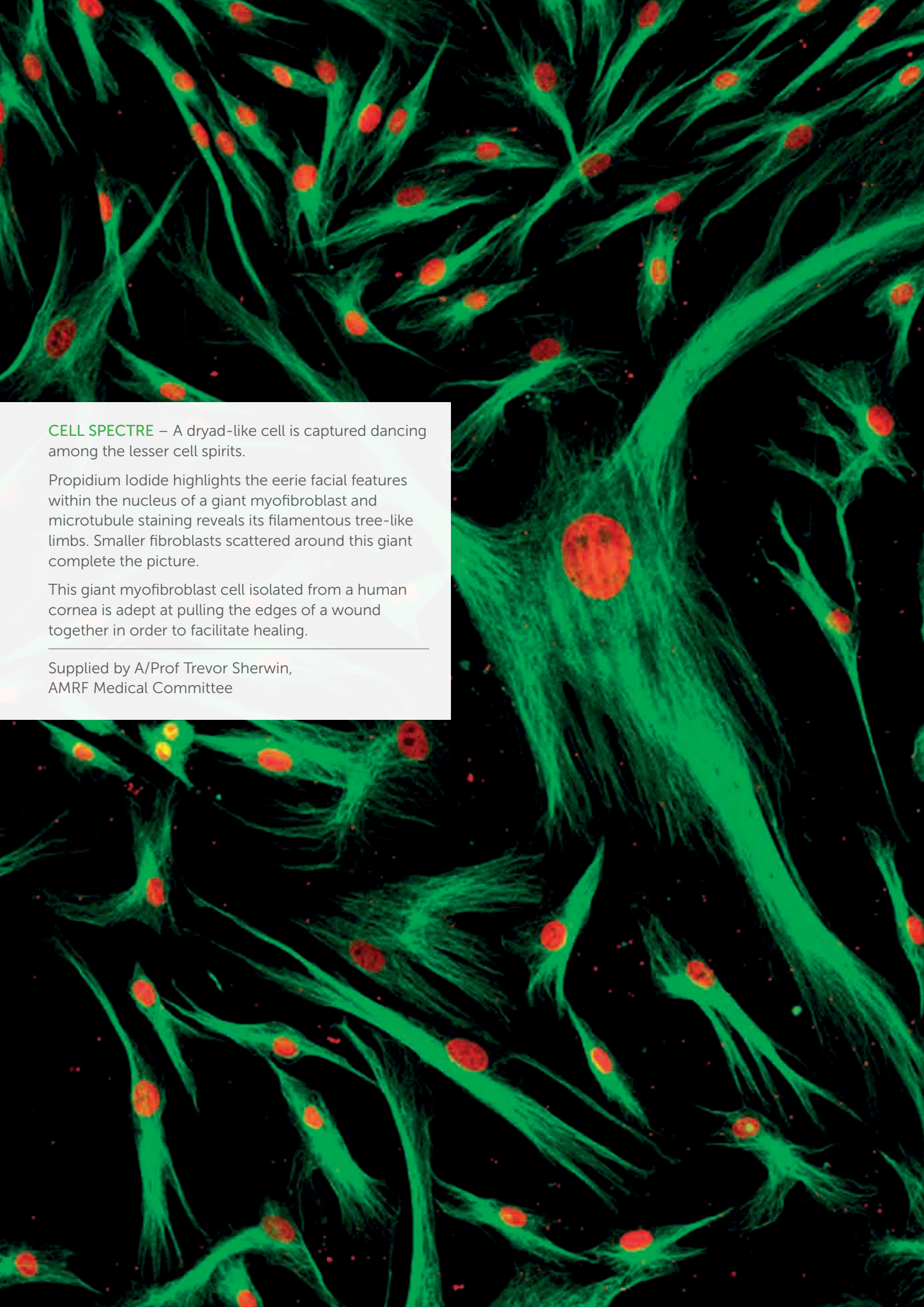
ANNUAL REPORT 2013



CELL SPECTRE – A dryad-like cell is captured dancing among the lesser cell spirits.

Propidium Iodide highlights the eerie facial features within the nucleus of a giant myofibroblast and microtubule staining reveals its filamentous tree-like limbs. Smaller fibroblasts scattered around this giant complete the picture.

This giant myofibroblast cell isolated from a human cornea is adept at pulling the edges of a wound together in order to facilitate healing.

Supplied by A/Prof Trevor Sherwin,
AMRF Medical Committee

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Charity Commission Registration Number: CC22674

President's Report & Medical Committee Report

YEAR ENDED 31 DECEMBER 2013

Jeff Todd.

Board Report

The AMRF believes that significant advances in medicine can only come about through quality research.

The Foundation strives to improve the health of New Zealanders through funding the highest quality medical research of all kinds - $52.2 million distributed since our inception in 1955. 2013 saw $4.45 million awarded in a single year - a significant lift from previous years, largely due to income from external funding and partners including Guardian Trust, Public Trust, Manchester Trust, and the Paul Stevenson Memorial Trust.

Building capacity and capability for a world-class research community in New Zealand is also at the heart of our philosophy and vision. We encourage personal research development gained through overseas experience but also support the repatriation of researchers home to New Zealand through the prestigious Goodfellow Repatriation Fellowship.

The Foundation is most grateful for all contributions made in 2013 and in particular for the generous annual endowment which covers all our operating expenses.

Our Executive Director, Kim McWilliams, and her small team have ensured the Foundation's operations have been conducted with professionalism and efficiency. The team has been tireless in its efforts and innovative in its approach to growing our capital base and in turn our support, in a very competitive philanthropic environment.

My personal thanks are extended to Trustees, Board Committee Chairs and Members who all contribute generously with their time and experience. In particular, I pay tribute to the Medical Committee, under the Chairmanship of Professor Peter Browett, whose demanding but essential work in reviewing applications for grants absorbs many hours in evaluation and assessment.

With the continuing commitment of Trustees, staff, members, grant holders, funding partners and donors, the future success of the Foundation is assured.

Jeff Todd

President

Prof Peter Browett.

Medical Committee Report

In a tough funding environment 2013 saw a 62% increase in the number of applications from previous years, with 252 applications (requesting $17.9 million) being submitted this year compared to 156 in 2012. Needless to say, many worthy applications were unable to be supported.

I would like to acknowledge the hard work and dedication of The Medical Committee who voluntarily provided their skills and expertise to assess all applications across six committee meetings held throughout the year. This resulted in the Committee and Board approving 78 grants overall. These grants support top quality research that will benefit all New Zealanders first and foremost, as well as having an impact on medical research and clinical practice worldwide.

A particular highlight was the awarding of post-doctoral fellowships (2), doctoral scholarships (4), and the prestigious Ruth Spencer Medical Research Fellowship (1). The Foundation has structured Fellowships carefully to build a package of support (salary, fees, working expenses and travel) for recipients, making them some of the most sought after opportunities in New Zealand.

I would like to thank the AMRF office staff for their support of the Medical Committee, and in particular the Research Programme Manager, Dr Hannah Gibbons, for her stewardship of the Grants Portfolio and development of the online AMRF Portal for grant submissions and assessment.

Peter Browett

Chair, Medical Committee
Professor of Pathology,
Department of Molecular Medicine and Pathology

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

DEVELOPING NEW TREATMENTS FOR AMBLYOPIA OR 'LAZY EYE' – BY DR BEN THOMPSON

Dr Ben Thompson.

Amblyopia, also known as 'lazy eye', is the leading cause of childhood visual impairment in the developed world and affects about one in 30 people. The most common types of amblyopia cause poor vision in one eye and stop the two eyes working together effectively. Amblyopia also doubles the lifetime risk of serious visual impairment which can occur if the good eye suffers damage or disease.

Counter-intuitively, lazy eye is not due to a problem with the eye itself, but is caused by abnormal brain development. If there is a mismatch between the images seen by each eye during early childhood, the visual areas of the brain may develop to process information from one eye abnormally. The mismatch may be the result of eye misalignment, unequal focus between the eyes or other impediments to vision such as a cataract. Irrespective of the cause, it is the disrupted brain development that leads to poor vision in the affected eye. This means that treating amblyopia involves changing the way in which the brain interprets information from the eyes.

The most common treatment for amblyopia is to cover the good eye with an eye-patch to encourage use of the amblyopic eye. Patching can be very effective when used in childhood but, many children find it difficult to wear the eye-patch and the treatment can last for many months or even years. Furthermore, patching is considered to be ineffective in older children and adults with amblyopia. This is because the mature brain is thought to lack the 'plasticity' or capacity for change, that is needed to learn how to use the amblyopic eye effectively.

With support from the AMRF, Associate Professor Ben Thompson and his colleagues have pioneered the development of novel approaches to the treatment of amblyopia in both adults and children. One of these new treatments takes a completely different approach to patching. Instead of forcing the use of the amblyopic eye, the new treatment encourages the two eyes to work together. This treatment can be given in the form of specially modified video games that can only be played if the two eyes cooperate. Initial studies have revealed highly promising results in both adults and children using this approach with improvements occurring in a matter of weeks.

A version of the treatment that runs on an iPod touch device is the focus of an international clinical trial led by Ben and supported by the Health Research Council. If the trial is positive, this technique could revolutionize the treatment of amblyopia.

Other promising approaches for adult patients include the application of safe, non-invasive brain stimulation techniques to the visual cortex and the combination of patching with Fluoxetine (Prozac), which has previously been found to reverse amblyopia in adult animals. Importantly, this research not only aims to improve vision, but is also designed to provide new insights into the mechanisms that control plasticity in the human brain. This means that studying the visual system could lead to the development of new treatment techniques that could be applied to a range of different brain disorders.

Q1. Please can you tell us a bit about yourself and how you came to be in this area of research?

I studied experimental psychology at the University of Sussex in the UK and developed a particular interest in the areas of the brain that support vision. I then took up a position as a research fellow at the University of California, Los Angeles, USA, where I studied the changes that occur in the brain when people with normal vision learn new visual skills. My next research position within the Department of Ophthalmology at McGill University in Canada provided me with the opportunity to apply what I had learnt about the brain to the development of new treatments for brain-based visual disorders such as amblyopia. When I arrived at the Department of Optometry and Vision Science at the University of Auckland in 2008, I established new research programs in the area of amblyopia treatment and human brain plasticity and have also maintained strong ties with my international colleagues.

Q2. How has AMRF funding allowed your research to evolve or progress to the next stage?

AMRF funding has played a central role in the development of my research. The first funding I received after joining the University of Auckland as a junior faculty member was an AMRF project grant. This grant allowed me to buy the equipment that I needed to establish my new laboratory and allowed me to hire an excellent full-time research assistant who helped me to drive the research forward. The success of these initial amblyopia treatment studies subsequently allowed me to secure funding from the Health Research Council and the Marsden Fund to grow the laboratory and further develop this area of research. The research funding environment in New Zealand is among the most competitive in the world and the funding I received from the AMRF early in my career allowed me to develop a research program that could deliver clinically relevant results and compete for government research funds.

Travel grants-in-aid from the AMRF have also allowed me to attend international conferences and present my work to international colleagues at their home institutions. I really can't emphasise enough the importance of international networks in establishing a successful research

program, particularly when the research has the long-term aim of contributing to international clinical practice. Conference attendance and presentations at international institutions allowed me to promote my research to an international audience and the networks I became a part of, allowed me to access international funding streams and build broad, productive collaborations. Attendance at international scientific conferences may be seen simply as a perk for researchers, but it is absolutely essential if New Zealand research is to make an impact on the international stage. Without travel support from the AMRF, establishing the networks required to launch projects such as the international clinical trial that I am currently leading, would not be possible. The clinical trial is called BRAVO (Binocular Treatment of Amblyopia using Video games) and includes study sites in Australia, Canada and Hong Kong. The video game based treatment for amblyopia being trialed was developed in close collaboration with colleagues in Canada.

Finally, doctoral scholarships from the AMRF have fostered new interdisciplinary research opportunities within the University of Auckland. I currently host two outstanding doctoral students in my laboratory who are AMRF scholarship recipients. Their research into visual development and plasticity brings together leading scientists and clinicians from the fields of ophthalmology, neonatology, paediatrics, neuropsychology and engineering.

Q3. Please can you tell us a bit about how your research outcomes are being used in New Zealand, and the benefit to New Zealanders from your research:

Our video game approach to treating amblyopia that is being assessed in the BRAVO trial may provide an alternative to patching for children and pave the way for adults with amblyopia to be treated. This is important as current data suggest that amblyopia affects over 155,000 people in New Zealand alone. Our initial smaller-scale studies have found that the video

game based treatment not only improves vision in the amblyopic eye, but can also restore 3D depth perception which requires both eyes to work together. In some cases, this was the first time that the patients had ever experienced 3D vision. In the longer term, current research into techniques that allow the adult brain to learn how to use an amblyopic eye may be applicable to a range of other neurological disorders that require skills to be relearned. I work closely with colleagues within the Centre for Brain Research at the University of Auckland to advance this goal.

Q4. Have there been significant overseas breakthroughs or collaborations resulting from your research? Please can you describe your team's contribution to the global research effort in your area:

Research is becoming increasingly globalised and research in the area of visual neuroscience is no exception. Collaborations within my laboratory include colleagues from over 20 different universities across 10 different countries including Canada, China, the USA and the UK. Work from my laboratory combined with work led by my international collaborators has started to change the way that we think about amblyopia and has generated a large number of international research programs investigating treatments designed to promote cooperation between the two eyes.

Q5. What is the next step in your research plan?

We are currently investigating the combination of multiple treatment approaches to see whether even greater vision improvements can be achieved in adults with amblyopia. I am also very interested in understanding the brain mechanisms that allow for vision to be improved and I am using a variety of brain imaging techniques to address this question. In addition, I am working closely with colleagues within the Department of Optometry and Vision Science, the Auckland Bioengineering Institute and the Liggins Institute on the development of new techniques for assessing vision in children that may allow for the early detection of vision and neurodevelopmental problems.

Q6. What is your greatest hope or dream for research in this field?

Patching has been the standard treatment for children with amblyopia for over 500 years and adults are currently left untreated. The development of new treatments that are effective for all ages and that involve fun activities such as playing video games would change the way we think about amblyopia and brain plasticity in general.

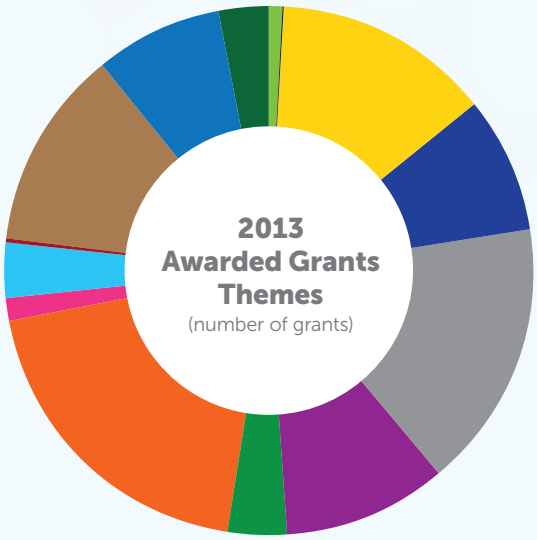
BECOME AN AMRF MEMBER

Join AMRF as an Annual or Life Member and receive reports and newsletters, and invites to special events and presentations.

See our website www.medicalresearch.org.nz or call us on (09) 923 1701 for further details.

GRANTS AWARDED

78 Grants Awarded Totalling $4,478,197



- Biomedical Imaging (2) | $5,000 0.1%
- Cancer (6) | $599,436 13.4%
- Cardiovascular Science (13) | $368,191 8.2%
- Cellular & Molecular Biology (10) | $728,100 16.3%
- Diabetes, Endochrinology, Metabolism & Nutrition (6) | $453,879 10.1%
- Musculo-Skeletal Science (3) | $163,232 3.6%
- Neuroscience (10) | $879,223 19.6%
- Other (6) | $52,144 1.2%
- Population Health (4) | $160,398 3.6%
- Pulmonary, Renal, Nephrology & Gastrointestinal Sciences (3) | $8,498 0.2%
- Reproduction, Development, Maternal & Newborn health (6) | $538,119 12.0%
- Sensory Sciences (7) | $357,710 8.0%
- Stem Cell Biology (1) | $126,000 2.8%
- Surgery (1) | $38,267 0.9%

$ Value each theme
% Total expenditure

Grants Awarded

PROJECT GRANTS

ORAL DEXTROSE GEL FOR PREVENTION OF HYPOGLYCAEMIA IN AT RISK NEWBORN INFANTS ($140,672 – 2 years) 1113012

Dr Jane Alsweiler, Prof Jane Harding, Dr Jo Hegarty
Dept of Paediatrics: Child and Youth Health, University of Auckland

Hypoglycaemia (low blood sugar) is the commonest metabolic condition in newborn babies, affecting up to 30% of babies born in Auckland hospitals. It frequently leads to neonatal intensive care unit admission and may cause long-term brain damage. Infants diabetic mothers are particularly at risk. Rates of maternal diabetes have quadrupled in NZ over the last two decades from 2% to 8%, with Polynesian and Māori women having the highest rates. There currently are no evidence-based strategies to prevent hypoglycaemia and its adverse consequences. We have shown that oral dextrose gel is effective in reversing established hypoglycaemia, halving NICU admission rates and improving rates of breastfeeding at two weeks. We now propose a trial investigating the effectiveness of dextrose gel for prevention of hypoglycaemia and its consequences in at risk babies. We will compare two different doses of dextrose gel, given on one or more occasions at feed times to those newborn babies at increased risk of having hypoglycaemia to determine a dose that will best prevent neonatal hypoglycaemia. We will determine whether dextrose gel prevents this common newborn condition with potential long-term health consequences. Such an intervention would revolutionise management of neonatal hypoglycaemia around the world.

TARGETING REPLICATION OF A HUMAN RESPIRATORY VIRUS ($139,620 – 2 years) 1113003

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

Respiratory Syncytial Virus (RSV) is the primary cause of serious respiratory disease in infants. The reported rates of RSV infection in New Zealand are almost twice that of Europe and the USA, and are particularly high for the Māori and Pacific Island population. There is no vaccine that prevents RSV infection, nor any effective therapy to treat infected individuals. We seek to understand how RSV replicates within human cells. RSV has complex replication machinery that creates the blueprint for new viral proteins, messenger RNA (mRNA), as well as copying the entire viral genome. However, the virus lacks a protein production system for translating viral mRNA into viral proteins, so it co-opts the system of the human host cell. For the viral mRNA to be processed by the host cell it must have specific chemical modifications. RSV and related viruses have unusual enzymes integrated into their replication machinery that carry out these mRNA modifications. We will isolate these enzymes using a technology developed in our laboratory, and carry out the first detailed molecular studies of their activity. The long-term goal is to develop new anti-viral agents that prevent RSV replication by targeting its unique mRNA modifying enzymes.

DANGEROUS DEBRIS ($139,447 – 18 months) 1113002

Prof Larry Chamley, Dr Qi Chen
Dept of Obstetrics & Gynaecology, University of Auckland

Preeclampsia affects approximately 3,000 New Zealand women and their babies annually. Preeclampsia causes potentially life-threatening high blood pressure in the mother and often requires the premature delivery of the baby to prevent the death of the mother or baby. Something from the placenta triggers preeclampsia but we do not know exactly what this is. We have evidence that dead cells from the placenta called syncytial nuclear aggregates may be this trigger but only if they died by a process called necrosis. We also have evidence that antiphospholipid autoantibodies, that are found in some women with preeclampsia, cause syncytial nuclear aggregates to die by necrosis. Why death by necrosis is so important in developing preeclampsia is unclear but this may be because necrotic syncytial nuclear aggregates display molecules called danger signals which cause the mother's blood vessels to tighten leading to the high blood pressure of preeclampsia. We will investigate whether antiphospholipid antibodies cause syncytial nuclear aggregates to display danger signals and whether syncytial nuclear aggregates from preeclamptic pregnancies display danger signals. Ultimately our goal is to understand how necrotic syncytial nuclear aggregates affect blood vessels and armed with that knowledge, we hope to improve treatments for women affected by preeclampsia.

REGULATION OF CREATINE SYSTEM IN NEURONS ($165,713 – 2 years) 1113024

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

This is produced by mitochondria, organelles that act as the power generator. Many neurodegenerative diseases have an energy deficit due to a loss of mitochondrial function. As a result, agents that promote mitochondrial activity have the potential to protect neurons. Creatine, a commonly used dietary supplement, is one such molecule as it enhances and maintains cellular energy levels. To be effective creatine must first be taken up into neurons and then be converted to phosphocreatine. These processes require a group of creatine system proteins. In this research we will investigate how the levels

of creatine system proteins are controlled and how they contribute to the energy levels and function of neurons. If ways can be found to up-regulate creatine system proteins this may lead to new strategies to enhance the neuroprotective effects of creatine for the treatment of human neurodegenerative diseases.

ANTIMALARIAL CONJUGATES ($23,600 – 2 years) 1113004

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

Malaria is a parasitic disease that has re-emerged as a growing human health hazard in the past few decades, affecting millions of people in Africa, Asia and South America. The drugs that are available for the treatment of malaria are becoming increasingly inadequate because of resistance and lack of patient compliance for multidrug treatment regimes. New, more efficient medications are urgently needed. We have recently discovered a class of natural products that exhibit moderate antimalarial activity and which, when synthesised and modified in certain ways yield drug candidates that effectively kill malaria in mammals. This project involves the synthesis and biological evaluation of new molecules based around our discovery, where we will optimize the parasite killing power of our current antimalarial while at the same time reducing the cost of its large scale manufacture. Our so-called multimodal antimalarials will provide proof of concept of combining therapeutics that kill and prevent reinfection with malaria into a single drug compound that not only is effective at disease treatment but also avoids resistance mechanisms and enhances patient compliance.

STUDIES OF THE EARLIEST EVENTS OF ALZHEIMER'S DISEASE IN THE ADULT HUMAN BRAIN ($114,416 – 2 years) 1113025

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

Alzheimer's disease (AD) causes severe memory loss and progressive dementia that directly affects 48,000 people in New Zealand and has a significant impact on the lives of a further 300,000 people in New Zealand. What causes this devastating disease is currently unknown in most instances with only approximately 10-15% of cases having an obvious genetic susceptibility. In brains affected by AD there is major cell death in the temporal and frontal lobes, however 8-10 years before this is evident the olfactory system (the smell centre) has already suffered significant cell death. To overcome the problem of major cell loss in AD, it will be important to intervene early before major cell loss has occurred, but to date the major studies of AD have focussed on end stage disease and not the initial brain changes. In the current project we aim to study the human olfactory system (where the disease begins), to determine what cell type are affected the most and to compare it with the textbook regions where damage occurs in AD. We will identify the earliest changes that occur in AD in the hope that future treatments might be helpful before depletion of brain cells has occurred in the brain.

FUNDED BY: W & WAR Fraser Fund

URATE AND BONE ($157,475 – 2 years) 1113015

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

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 the development of thin bones (osteoporosis) and fractures. This laboratory study aims to understand how urate exerts this protective effect. We will study the effects of urate on the function of bone-forming cells (osteoblasts) and cells that control the breakdown of bone (osteoclasts). We will also study the effects of medications that reduce urate levels on bone structure. If urate does indeed directly act on bone cells to increase bone density and reduce fracture risk, these observations may have important clinical implications in guiding blood urate targets in people treated for gout (the most common form of inflammatory arthritis), understanding patterns of bone disease in people with gout, and, in the long-term, identifying new therapeutic strategies for prevention of osteoporosis.

MYELINATION FAILURE IN THE PRETERM BRAIN ($114,433 – 2 years) 1113021

Dr Justin Dean
Dept of Physiology, University of Auckland

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. We have new evidence that a molecule called hyaluronan is highly up-regulated in preterm ischemic white matter injury, and that hyaluronan may be the cause of failure of oligodendrocytes to produce myelin. In this proposal, we will examine how hyaluronan triggers myelin deficits in the preterm brain. This new

Grants Awarded continued

knowledge will further our understanding of the causes of cerebral palsy in preterm infants, and determine whether blocking hyaluronan is a potential treatment strategy in this large group of children.

DIABETIC CATARACT ($59,061 – 18 months) 1113006

Prof Paul Donaldson, Miss Irene Vorontsova
School of Medical Sciences, University of Auckland

Cataract occurs earlier in patients with diabetes, and is associated with a higher rate of surgical complications. Due to the increasing incidence of diabetes, a cataract epidemic is looming that will place an economic burden on the health system. Research efforts to alleviate this burden have focused on finding alternative medical therapies to delay cataract progression and reduce the need for surgery. The Molecular Vision Laboratory at the University of Auckland has shown that dysfunction in the ability of lens to regulate cell volume is an underlying cause of diabetic cataract. On-going work by the Auckland group has identified the key membrane transport proteins that effect changes in lens cell volume. More recently a PhD student in the laboratory, Irene Vorontsova, has identified the regulatory machinery that modulates the activity of these transporters and which therefore ultimately determine the transparency of the lens. Ms Vorontsova is a former recipient of the AMRF's Senior Scholarship and in this current application funds are requested to continue Ms Vorontsova's work into how these regulatory pathways are disrupted in the diabetic lens. This work will determine whether these regulatory pathways are potential targets for development of therapies to combat the diabetic cataract epidemic.

FUNDED BY: The Hugh Green Diabetes & Breast Cancer Research Fund

THE TUI STUDY ($78,500 – 2 years) 1113008

Prof Cindy Farquhar, Dr Emily Liu, Miss Nicola Arroll
Dept of Obstetrics & Gynaecology, University of Auckland

Up to 20% of New Zealanders will experience infertility at some point in their lives. The TUI study aims to evaluate the effectiveness of a fertility treatment called intrauterine insemination (IUI) with stimulation. IUI is especially popular in New Zealand as couples with unexplained infertility cannot access the publicly funded fertility clinics unless they have been infertile for five years. As a result many women decide to pay for one to two cycles of stimulated IUI while they are waiting to meet the criteria for public funding. IUI with ovarian stimulation involves the women taking medication to stimulate ovulation before introducing sperm directly into the uterus in the hope of aiding conception. Currently knowledge around the effectiveness of this treatment in women with unexplained infertility and low chance of pregnancy (less than 30% chance) is not extensive. If this randomised controlled trial demonstrates that intrauterine insemination with stimulation is effective then this would provide evidence for a less invasive and cost effective alternative to In vitro fertilisation for women with unexplained infertility.

CB2 IN THE DISEASED HUMAN BRAIN ($66,792 – 1 year) 1113011

A/Prof Michelle Glass, Dr Scott Graham
Dept of Pharmacology, University of Auckland

Cannabinoid CB2 receptors have been suggested to be an appealing target for neuroinflammatory disorders as many believe them to be found only on immune cells. However, their distribution is actually highly controversial with some groups reporting widespread neuronal distribution, while others see little evidence for CB2 in the brain. Part of the reason for these discrepancies is that the antibodies used to detect this protein are not entirely specific. Furthermore, many of the assumptions about CB2 expression in the brain are based on animal studies and may not represent the situation in the human brain. As many drug companies are aiming to bring CB2 directed therapies onto the market, it is critical that the localisation of the receptor be accurately determined. We have recently developed a sensitive method for determining the expression of CB2 in the normal healthy brain, which we now wish to apply to diseased brains from the Human Brain Bank.

ACCELERATED BEP STUDY ($59,105 – 2 years) 2113019

Dr Fritha Hanning, Dr Peter Fong, Dr Reuben Broom
Auckland Regional Cancer & Blood Service, Auckland City Hospital

Testicular cancer and closely related cancers called germ cell tumours are the most common cancer in men aged 16 to 45. Despite this, it receives very little attention or publicity, in part due to an understandable reluctance of men in this age group to discuss their cancer journeys. Thankfully for those men who are able to detect their cancer early, there are excellent outcomes with treatment ranging from 98-99% cure rates for men with stage one disease (confined within the testicle) to 90-95% for men with good prognosis metastatic cancer (cancer which has spread to other parts of the body). Unfortunately for men whose disease is more extensive and aggressive, there is still a significant chance of dying from the cancer. The research study 'Accelerated BEP' aims to improve outcomes for men whose cancer was not diagnosed before it reached this more serious stage. It is looking at whether changing the timing of an established chemotherapy treatment will improve survival. A positive outcome from this study would mean an increased cure rate for this group of young men and an increased chance of them living full and productive lives.

FUNDED BY: Sir Lewis Ross Fund and the Rose Richardson No. 1 Trust

REDUCING FGF23 IN CHRONIC KIDNEY DISEASE ($133,166 – 1 year) 3113014

Dr Christopher Hood, Mr Mark Marshall, Dr Joanna Dunlop
Renal Dept, Middlemore Hospital

Chronic kidney disease (CKD) is a major public health issue which is both very common and harmful, with a similar magnitude of effect as diabetes. This is mainly due to greatly increased levels of cardiovascular disease (CVD) in CKD patients. Recent ground-breaking research has identified a causative pathway linking CKD and CVD, via increased levels of a hormone called FGF23. FGF23 acts directly on the heart to cause enlargement of heart cells, which results in cardiac failure and increases the risk of sudden cardiac death. Multiple research efforts attempting to reduce FGF23 levels in CKD all use intensive hospital-based treatments of specialised diets or treatment regimens unsuited to widespread "real world" use. Our study aims to demonstrate that a simple treatment with niacinamide (a metabolite of vitamin B3) will significantly reduce FGF23. Such a simple treatment could transform the field, taking it away from clinical trials and specialist clinics to a primary care-based intervention, applicable to the wider CKD population. Our trial aims to investigate whether FGF23 is reduced by niacinamide treatment. A successful result would support larger studies aimed at demonstrating that niacinamide can prevent the cardiac enlargement and increased cardiovascular disease seen in people with CKD.

TROPHOBLAST STEM CELLS ($50,000 – 18 months) 1113005

Dr Jo James, Prof Larry Chamley
Dept of Obstetrics & Gynaecology, University of Auckland

The placenta is the baby's life-support system in utero, and its formation and function in early pregnancy is crucial for pregnancy success. Inadequate placental development results in pregnancy disorders from conception to birth including miscarriage, preeclampsia (high blood pressure in pregnancy) and intrauterine growth restriction (small babies), which together affect around 15,000 pregnancies in NZ each year. Despite its importance, we understand very little about how the human placenta develops. This research aims to address this problem by studying the stem cells from which the placenta is formed. The placenta is composed of specialised cells called trophoblasts, which form different populations each critical for pregnancy success, but we do not understand how these populations arise. We have isolated cells that are likely to be trophoblast stem cells from early placental samples, and are characterising these cells in order to develop trophoblast stem cells for use in the laboratory. This will allow us to study what regulates the formation of different trophoblast populations. This research will help us identify potential underlying causes of pregnancy disorders and may lead to new therapies for pregnancies with poor placentas.

EFFECTS OF PARKINSONIAN TOXINS ON THE LOCUS COERULEUS ($103,000 – 2 years) 1113007

Prof Janusz Lipski, Mr Andrew Yee, Dr Peter Freestone, Dr Ji-Zhong Bai
Dept of Physiology & Centre for Brain Research, University of Auckland

Parkinson's disease (PD) is one of the most common degenerative brain disorders leading to motor deficits such as tremor in hands, slowness of movement, muscle stiffness and gait disturbance. 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 cause additional disability and severely impact the quality of life of those affected with PD. Previous research indicates that at least some of these non-motor symptoms are due to degeneration of nerve cells in the Locus Coeruleus (LC), but the cellular mechanism of this damage is not known. Remarkably, degeneration of the LC can exceed damage of the Substantia Nigra pars compacta (SNc) associated with the 'classical' motor symptoms of the disease. Our study, conducted on isolated animal brain tissue, will test and compare the effects on LC neurons of two environmental toxins/pesticides which have been implicated in the pathogenesis of some cases of PD: rotenone and MPP+. We will also compare the effects evoked in LC neurons with the responses induced in SNc neurons, and a further group of neurons which is not affected in PD. This research will advance our understanding of the mechanisms of action of parkinsonian toxins on neurons vulnerable in PD, and should help to elucidate the complex relationship between the motor and non-motor symptoms in this debilitating disorder.

FUNDED BY: Angus Family Trust

Guardian Trust

SHON RECEPTOR IDENTIFICATION ($159,960 – 2 years) 1113022

Dr Dong-Xu Liu, Dr Christopher Squire
Liggins Institute, University of Auckland

Breast cancer is a major health issue, being the most common malignancy and the leading cause of cancer deaths among New Zealand women. Each year approximately 3,000 women are diagnosed with breast cancer and more than 650 die from the disease. We have identified a novel secreted oncoprotein, called SHON, in the blood. SHON plays an important role in breast cancer. Its expression status in breast tumours predicts the response of patients to anti-oestrogen therapies. We will identify the mechanism by which SHON regulates cellular function by finding proteins to which it binds and signalling pathways that it activates. These studies will provide an important contribution to our understanding in the area of secreted oncogenic proteins and is likely to lead to better treatment for breast cancer in the future.

FUNDED BY: Breast Cancer Research Fund

Grants Awarded continued

LONG QT SYNDROME AND HYPERTROPHIC CARDIOMYOPATHY GENE ANALYSIS ($50,000 – 18 months) 2113017

Dr Donald Love, Dr Jonathan Skinner, Dr Ivone Un San Leong
Diagnostic Genetics, LabPlus

Congenital long QT syndrome and hypertrophic cardiomyopathy are life-threatening cardiac disorders that are the most common causes of sudden death in 1 – 40 year olds in New Zealand, with an incidence of 1 in 4,500 and 1 in 500, respectively. These diseases commonly present in childhood and young athletes, and are characterised by unexplained fainting episodes and dangerously fast heart rates that could cause sudden death. The genotyping of patients with these disorders has greatly assisted both with family screening and individualizing clinical management. The current sequence-based screening strategy for mutations in patients is labour intensive. Critically, developments in Massively Parallel Sequencing (MPS) technology has made it possible to screen scores of genes for mutations, or the entire coding potential of the human genome (termed whole-exome sequencing, WES), in parallel. This project will establish MPS technology in the clinical diagnostic arena of New Zealand (with a focus on cardiac disorders), and will therefore improve the current method and provide an enhanced national service for patients.

TECHNOLOGY AND CARDIAC REHABILITATION ($153,003 – 2 years) 1113020

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

Exercise is essential to aid recovery from a heart attack, however adherence to regular exercise is low. In this trial we will compare the effectiveness of home-based monitored exercise using mobile phones and monitoring technology to existing supervised exercise cardiac rehabilitation. 230 participants will be allocated at random to 12 weeks standard supervised exercise cardiac rehabilitation or to the new mobile phone programme. Assessments will compare physical fitness, and change in risk factors associated with heart disease between the two groups. This approach has potential to improve the delivery of cardiac rehabilitation services in New Zealand for those who need it.

FUNDED BY: AC Horton Estate

OXYGEN IN DISEASE KIDNEYS ($160,000 – 2 years) 1113016

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

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 are ill-defined. We hypothesize that low oxygen levels in the kidney is central in the pathogenesis of kidney disease. This project will examine how and when low oxygen levels in the kidney can play a major role in driving disease progression and whether improving kidney oxygenation can prevent kidney disease. Investigation of kidney oxygen regulation has been hindered because of an inability to measure tissue oxygen for long periods of time. Using our world first technology which allows wireless measurement of kidney tissue oxygen in unrestrained rats we have solved this problem. We will investigate, using this technology and unique expertise, the sequence of events that lead to reduced kidney tissue oxygen in kidney disease. We aim to identify when and which mediators/controllers of long-term regulation of kidney oxygen precedes and/or is a prerequisite for the progression of disease. This will reveal causation that will assist in optimising the appropriate, and novel, treatment strategies. We believe this will ultimately have a major impact in clinical practice, making it a very promising and timely subject.

REVERSAL OF MULTI-DRUG RESISTANCE BY DRUG-PHYTOCHEMICAL COMBINATION THERAPY ($159,293 – 2 years) 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 chemotherapy in pancreatic cancer is the development of multi-drug resistance due to up-regulation of various efflux pumps in the cancer cells. The latter can efficiently remove the drug from the cell, thus causing the drug to lose its effect. Our aim is to investigate a novel bi-functional liposomal delivery system which contains the anticancer drug plus curcumin, an inhibitor of the efflux pump. This combinational liposome will more effectively target and retain the active drug within the cancer cell, thus overcoming multidrug resistance, and also minimising any toxic side effects.

IMPROVING THE SURGICAL DRAINAGE OF NECROTISING PANCREATITIS ($28,761 – 2 years) 1113013

Dr Anthony Phillips, Prof John Windsor, Dr Harvey Ho, Dr Lisa Brown
School of Biological Sciences, University of Auckland

Acute pancreatitis is due to inflammation of the pancreas gland. This can develop into a very severe form in which a portion of the pancreas gland dies and becomes infected. This has a high mortality for patients, and is best treated by draining the area of infection by passing a drain through the skin into the dead, infected pancreatic tissue. Unfortunately, these drains work in less than 50% of patients and regularly block with the pancreatic tissue, requiring patients to undergo a major open operation to remove the dead tissue, which increases the risks of complications and death. This research aims to reduce the occurrence of drain blockage, by finding an enzyme solution that could be flushed down the drains to dissolve the pancreatic tissue. There is also the opportunity to

improve drain design to keep it open and to make it easier to drain the infected tissue. The optimization of the drainage of infected pancreatic tissue will reduce the burden of this disease on patients, reduce the requirement for major open surgery, and reduce costs to the health system.

MAGGOT SECRETIONS PROMOTE WOUND HEALING?
($28,761 – 1 year) 1113023

Dr Anthony Phillips, Dr Cherie Blenkiron
School of Biological Sciences, University of Auckland

The use of maggots for a medicinal purpose is age-old. The maggots, from the green bottle blow-fly, secrete a potent cocktail of molecules which kill infecting bacteria, digest away dead tissue and even directly promote wounds to heal. We intend to look at the activity of maggot secretions on a range of target cells to give us a greater understanding of its biological effects. With better understanding of its bioactivity we hope to exploit specific components for use in the clinic as new classes of treatment for a range of surgical wounds.

Gcn2 INTERACTOME
($66,630 – 2 years) 4113010

Dr Evelyn Sattlegger, Miss Su Jung Lee
Institute of Natural and Mathematical Sciences, Massey University

The enzyme Gcn2 is involved in many life-affirming biological functions, such as proper food selection, viral defence, memory, and overcoming stress and starvation. Consequently, Gcn2 is a highly relevant protein, for medicine especially as research has linked Gcn2 to various diseases/disorders such as aberrant feeding behaviour, Alzheimer's, cancer, and impaired viral defence. Given that these diseases/disorders significantly impact on health and quality of life, this underscores the need to find drugs for their treatment. However, in order to prevent unwanted side effects, measures are necessary that only treat the specific Gcn2 function that went awry. For this we first need to fully understand how Gcn2 is kept in check in the cell. Although Gcn2 is a topic of research world-wide, there remains one significant knowledge gap central to understanding Gcn2 function: the comprehensive identification of proteins that bind to Gcn2, and thereby control Gcn2. These proteins are promising targets for pharmaceutical treatments to modify specific Gcn2 functions that lead to a particular Gcn2-associated disease/disorder. The PI's research team is in a unique position to identify these Gcn2 binding proteins, and to spearhead the first characterisation of these proteins, as the relevant experimental procedures have been established in her lab.

THE NEUROPHYSIOLOGICAL BASIS OF THE ADAPTATION LEVEL THEORY OF TINNITUS
($85,508 – 1 year) 1113028

Dr Grant Searchfield, Prof Dirk De Ridder, Dr Cathy Stinear, Prof Ian Kirk, Mr Giriaj Singh Shekhawat
School of Population Health, University of Auckland

Tinnitus ("ear and head noise") is a highly prevalent condition affecting approximately 15% of the population. Severe tinnitus can lead to disruption of work, social activities and sleep; and lead to anxiety and depression. There is a pressing need for effective therapies to help solve this common problem. In the last decade there have been tremendous advances in our understanding of the mechanisms underlying tinnitus but effective treatments for tinnitus remain elusive despite these advances in knowledge. Tinnitus can be temporarily reduced or eliminated by sound stimulation and non-invasive brain stimulation but only in some people, some of the time. Tinnitus is complex; studies of brain activity indicate auditory, memory, attention and emotional parts of the brain work together to create tinnitus. These studies have led to a "Neurophysiological Network" model of tinnitus. Recently an "Adaptation Level Theory" model of hearing has explained how memory, attention and emotion might contribute to tinnitus magnitude. The proposed research will examine how the two models of tinnitus interrelate. We will measure brain activity (Electroencephalography, EEG) and tinnitus loudness before, during, and after sound stimulation and non-invasive stimulation of different brain areas. The studies should identify new targets and means for treating tinnitus.

FUNDED BY: Jean Cathie Research Fund

Guardian Trust

CANNABINOID DRUGS FOR THE TREATMENT OF TINNITUS
($80,976 – 1 year) 7113027

Prof Paul Smith, Dr Yiwen Zheng
Dept of Pharmacology and Toxicology, University of Otago

Tinnitus is a debilitating neurological disorder in which a person hears sounds that do not physically exist. Approximately 7% of the New Zealand population is estimated to suffer from tinnitus at least 50% of the time and the condition becomes more prevalent with age. Tinnitus substantially reduces the quality of life, resulting in an inability to concentrate and increased anxiety. Approximately 50% of tinnitus sufferers also suffer from depression. Unfortunately, there are few effective treatments. We have shown that receptors in auditory brain regions for chemicals known as 'cannabinoids', undergo changes during tinnitus. We therefore propose to test whether a cannabinoid drug known as 'Sativex', might be beneficial in the treatment of the disorder. First, we will determine whether it reduces the perception of tinnitus. Second, we will measure the way in which it alters brain activity in the brain regions which normally exhibit increased excitability during tinnitus. Since Sativex is already available for prescription in New Zealand, if we obtained evidence indicating that it could be useful in the treatment of tinnitus, this drug could potentially be used with a minimal delay.

FUNDED BY: Jean Cathie Research Fund

Guardian Trust

Grants Awarded continued

THE SYNAPTIC BASIS OF AUTISM ($21,048 – 1 year) 1113018

Dr Charlotte Thynne
Dept of Physiology & Centre for Brain Research, University of Auckland

Autism Spectrum Disorders are complex disorders that are diagnosed based on behavioural symptoms including social and cognitive impairments, communication difficulties and repetitive behaviours. Interestingly, many of the genes that have been implicated in Autism encode proteins found at excitatory synapses in the brain. These include genes which encode postsynaptic scaffolding proteins as well as presynaptic calcium channels and calcium dependent mechanisms. This work aims to determine if there is a functional sub-cellular link between postsynaptic scaffolding proteins and presynaptic calcium channels, which could explain the shared features observed in Autism patients carrying mutations in the genes which encode these separate entities. Using electrophysiology techniques, I will examine how ProSAP2, a postsynaptic scaffolding protein implicated in Autism, regulates presynaptic calcium channel function and how autism-associated mutations in this protein affect this regulation. These experiments have the potential to determine how the function and plasticity of excitatory synapses may be disrupted in Autism, leading to interference with cognitive function and behaviour.

GENETICS OF ANTERIOR CORNEAL DYSTROPHY ($138,968 – 18 months) 1113001

Dr Andrea Vincent, A/Prof Trevor Sherwin, Prof Phil Crosier
Dept of Ophthalmology, University of Auckland

Inherited disorders affecting the clear front window of the eye are known as corneal dystrophies. Members of a unique NZ family have significant recurrent episodes of eye pain from childhood, caused by the front surface of the cornea falling off, which often leads to progressive scarring. The cause of this rare disease is unknown, however our recent work shows this disease is due to one of two gene mutations on chromosome 10. Our aim is to understand the normal role of these genes, and the consequence of changes to these genes, in corneal health and disease. We will look at the two protein products of these genes in donor corneas to establish where the proteins sit within the outer-most layer of corneal cells, and what stimuli, e.g. stress or trauma, may change their production. We will then establish disease models in zebrafish by introducing the disease gene(s) into the developing zebrafish embryo, to see the effect on the zebrafish cornea. Using this animal model of a rare genetic disorder will help identify an underlying cause for a more common condition, recurrent corneal erosion, and will help target effective treatments for corneal wound healing, both accidental, and due to surgical interventions.

HOMING IN ON THE EPITOPE TARGETS FOR NR1 ANTIBODIES ($138,076 – 2 years) 1113009

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

The NMDA receptor in the brain plays an important role in functions such as learning and memory. Over-activation or dysfunction of the NMDA receptor that occurs in certain neurological diseases causes neuronal cell death or can affect learning and memory making this receptor a key target for therapies. Traditional NMDA receptor blockers that aim to prevent the deleterious effects associated with NMDA receptor dysfunction are associated with adverse side-effects in humans which limits their usefulness. We have shown that antibodies to the NR1 subunit of the NMDA receptors can alter the function of NMDA receptors leading to improved learning and memory, and resistance to experimentally-induced brain insults in rats. Anti-NMDA receptor encephalitis, a disease associated with seizures and memory loss in humans is mediated by NR1 antibodies that could be binding to a region of the NR1 protein that is different to our cognitive-enhancing and protective NR1 antibodies. Here, we use rat models to help distinguish the parts of the NR1 subunit important for generating NR1 antibodies that produce beneficial and detrimental effects on cognition and neuroprotection. These results will contribute to the development of a new class of safe therapies applicable for a broad range of neurological conditions.

NAMED FELLOWSHIPS

GOODFELLOW REPATRIATION FELLOWSHIP

DEVELOPING ZEBRAFISH *ETV6* MODELS OF ACUTE MYELOID LEUKAEMIA FOR CHEMICAL SUPPRESSOR SCREENS ($376,437 – 2 years) 1413001

Dr Andrew Wood
Dept of Molecular Medicine and Pathology, University of Auckland

Acute Myeloid Leukaemia (AML) is a blood cancer that is frequently fatal despite intensive chemotherapy and stem cell transplantation. Spelling mistakes accumulate in the DNA instructions that control how a cell behaves with the result that white blood cells keep reproducing until they overtake the body leading to clinical symptoms. By sequencing leukaemias from many people we have built up catalogues that list the various spelling mistakes, but it is not always clear how to translate this knowledge into better treatments. In children with AML the gene *ETV6* is frequently mutated, and although a lot is known about this gene in health and other cancers, very little is understood about why it makes AML in children so hard to cure. In this research we aim to find out how *ETV6* mutations work by introducing them into zebrafish. We hope the mutations will change the way leukaemias grow in fish, and that by studying this we

will learn the leukaemia's weak spot. Then we will use robots to treat thousands of zebrafish with thousands of drugs to see if any kill *ETV6* leukaemia. If successful, this study will identify compounds that can be used to better treat *ETV6* driven leukaemias in patients.

RUTH SPENCER MEDICAL RESEARCH FELLOWSHIP

MANAGEMENT OF NEONATAL HYPERGLYCAEMIA ($257,333 – 3 years) 1413002

Dr Kathryn Williamson
Newborn Services, Auckland City Hospital

Babies who are born very preterm have a high risk of suffering brain damage. High blood sugar levels (hyperglycaemia) are common in these very small babies, and are associated with poor outcome. Hyperglycaemia is usually treated with insulin, but in very small babies the correct dose of insulin can be difficult to determine and babies' insulin requirements can fluctuate over a short period of time. This means that sometimes the babies' blood sugar level can fall too low (hypoglycaemia). Unfortunately, hypoglycaemia can put babies at further risk of brain damage. A computer program has been developed to help keep blood sugar levels in a safe range for preterm babies treated with insulin. We will determine if this computer program can reduce the incidence of hypoglycaemia, and also whether it improves growth and later development. If effective, this computer program will be incorporated into routine care of preterm babies in New Zealand and worldwide, potentially reducing the burden of brain damage after preterm birth.

FUNDED BY: Ruth Spencer Trust

Guardian Trust

DOCTORAL SCHOLARSHIPS

BARBARA BASHAM DOCTORAL SCHOLARSHIP

MATERNAL THERAPY AND THE FETUS ($126,000 – 3 years) 1213003

Mr Christopher Lear
Dept of Physiology, University of Auckland

Brain injury after preterm birth now contributes more than a third of all cases of cerebral palsy. We now know that even babies born prematurely without brain injury have a high risk of long-term disability and learning difficulties. Mothers who are about to deliver prematurely are almost universally given treatments such as steroids and magnesium sulphate to reduce the risk of death and many newborn complications after preterm birth. Given how often our youngest and most vulnerable infants are exposed to these treatments, it is vital to understand their effects on the preterm brain. We have recently shown that a clinical course of maternal steroids triggers transient abnormal brain activity in preterm animals, and can worsen injury during exposure to low oxygen levels. The long-term effects are unknown. In this study, I will examine the long-term impact of exposure to maternal steroids on brain activity and structure, how timing of treatment affects the response to low oxygen, and finally, whether magnesium sulphate treatment can alleviate the adverse effects of steroids on the brain. This will be providing critical new information to help guide the clinical treatment of women at risk of preterm delivery.

FUNDED BY: Barbara Basham Medical Charitable Trust

Guardian Trust

MOLECULAR IMAGING OF LENS CATARACT ($126,000 – 3 years) 1213004

Mr Mitchell Nye-Wood
School of Medical Sciences, University of Auckland

Cataract is primarily a disease of old age and Age-Related Nuclear (ARN) cataract is the leading cause of blindness in the world today. ARN cataract is characterised by irreversible protein modifications in the centre or nucleus of the lens. Antioxidants in the young lens usually provide protection against this oxidative damage but an age-dependent decline in antioxidants, specifically in the lens nucleus, allows damaged protein to accumulate, eventually leading to protein precipitation, loss of transparency and cataract formation. In this study we investigate the mechanistic link between the antioxidant decline in the lens nucleus, oxidative damage to lens proteins and the loss of lens transparency using an animal model of ARN cataract. To achieve this, changes in the distribution of antioxidants and oxidative damage to lens proteins will be spatially mapped using imaging mass spectrometry, a technique that can identify and localise small molecules and large proteins in tissue sections. The effect of these biochemical changes on lens transparency will then be determined by measuring the optical properties of lens. Our study of how antioxidant depletion specifically in the lens nucleus affects overall lens transparency, will aid our efforts to develop medical therapies to delay the onset of ARN cataract.

MESENCHYMAL STEM CELLS AND IUGAR ($126,000 – 3 years) 1213001

Miss Megan Alexander
Dept of Obstetrics & Gynaecology, University of Auckland

A healthy placenta is the cornerstone to a successful pregnancy and delivery of a healthy baby. Insufficient placental development can lead to life-threatening pregnancy disorders such as pre-

Grants Awarded continued

eclampsia (hypertension in pregnancy) and intrauterine growth restriction (IUGR, small babies), which have lifelong consequences. We currently know surprisingly little about the pathophysiology of pregnancy disorders, and have no effective treatments to remedy these conditions. Recent trials in other organ systems have highlighted the therapeutic potential of mesenchymal stem cells (MSC) for a range of applications. In the placenta, MSC are present throughout gestation and may contribute to creating an adequate vascular network, which is key for foetal growth. Therefore, MSC provide a promising target to improve placental vascularisation in IUGR pregnancies. This project aims to explore this potential by determining how MSC may contribute to the pathophysiology of IUGR, and whether transplantation of MSC into placentae can stimulate placental angiogenesis via direct engraftment into the placental vasculature or by paracrine mechanisms. This proof of principle work will allow the future development of MSC as a therapy for failing placentae, helping improve the lives of around 5,000 babies and their mothers affected by IUGR each year.

HENRY COTTON DOCTORAL SCHOLARSHIP

THE SYNAPTIC BASIS OF HUNTINGTON'S DISEASE ($126,000 – 3 years) 1213002

Mr Wojciech Ambroziak
Dept of Physiology & Centre for Brain Research, University of Auckland

Currently one in five New Zealanders are affected by neurological diseases and as the population ages this number will considerably increase. All neurological diseases have direct or indirect effects on synapses in the brain. This project is to determine the source of synapse dysfunction in Huntington's Disease (HD). HD is one of the most debilitating, incurable adult onset diseases with very dramatic course. Studies on HD mouse models have shown that an increase in NMDA receptors located outside of the synapse causes early synapse dysfunction that may underlie the cognitive and motor deficits seen in HD. A protein called SAP97 plays distinct roles in regulating receptor distribution within synapses, with aSAP97 regulating synaptic receptors versus bSAP97 regulating receptors outside of the synapse. Recent data suggest that this protein is a causative agent in the early pathogenesis of HD. The aims of this PhD project are to determine the role of each SAP97 isoform in the changes in NMDA receptor localisation in a cellular model of HD and if SAP97 isoform expression levels can be specifically targeted to rescue normal receptor distribution and synapse function in animal model, thus whether SAP97 isoforms are a potential therapeutic target.

FUNDED BY: Henry Cotton Charitable Trust

Guardian Trust

POSTDOCTORAL FELLOWSHIPS

EDITH C. COAN RESEARCH FELLOWSHIP

FUNCTIONAL CHARACTERISATION OF CANNABINOID RECEPTOR SNPS IMPLICATED IN MENTAL ILLNESS ($196,000 – 2 years) 1313001

Dr Natasha Grimsey
Centre for Brain Research, University of Auckland

Mental illnesses such as depression, bipolar disorder and schizophrenia affect around 16% of New Zealanders. Most of these conditions are difficult to diagnose and treat effectively. Continued research is required to better understand these disorders and develop new medicines. The mind-altering properties of cannabis have been recognised for centuries, but the proteins in the brain that allow cannabis to exert its effects have only been identified in the last two decades. These proteins are called Cannabinoid Receptors 1 and 2, and as well as responding to cannabis these control many normal bodily functions. All the proteins in our bodies are produced from DNA blueprints. Slight differences in these instructions between individuals can result in subtly different versions of the same protein which might work differently. A few specific versions of Cannabinoid Receptor 2 are more common in patients suffering from mental illness than in the general population. This may indicate that these versions play a role in these diseases. In this research I plan to investigate what is different about the function of these versions of the Cannabinoid Receptor. This information will provide new insight into the causes of mental illness and may assist with designing new therapies.

FUNDED BY: Edith C Coan Trust

Guardian Trust

DAVID AND CASSIE ANDERSON RESEARCH FELLOWSHIP

MATERNAL DIET INDUCED PROGRAMMING OF OFFSPRING IMMUNE FUNCTION ($186,640 – 2 years) 1313003

Dr Clare Reynolds
Liggins Institute, University of Auckland

Unbalanced maternal nutrition, whether it be over-nutrition or under-nutrition, predisposes or "programs" offspring to obesity, type-2 diabetes and cardiovascular disease in later life. These conditions are associated with chronic low-grade inflammation, however little is known in regards to the impact of maternal diet-induced programming of the offspring immune system and its subsequent impact on metabolic function and indeed chronic disease later in life. We aim to investigate obesity-induced inflammation during pregnancy and subsequent long-term offspring disease in an established rat model of maternal diet-induced obesity. We will assess the origins of inflammation

in mothers and offspring by characterizing inflammation in the placenta, bone marrow and cells of the immune system. Furthermore we will determine the effectiveness of the anti-inflammatory lipid c9, t11 conjugated linoleic acid (CLA) as a therapeutic option for the reversal of maternal over-nutrition induced developmental programming. This project will allow us to establish the importance of immune mediators in developmental programming of obesity and metabolic complications and potentially develop a viable anti-inflammatory nutrient based therapeutic strategy for combatting the origins of metabolic disease.

FUNDED BY: David and Cassie Anderson Medical Trust

Guardian Trust

OTHER GRANTS AWARDED

AMRF HEALTHEX EMERGING RESEARCHER AWARD – ($5,000 Travel Award) 6713001

Miss Lucy Goodman
Dept of Physiology, University of Auckland

To attend the 9th FENS Forum of Neuroscience, Milan, Italy 5-9 July 2014 and to visit the laboratories of her Primary Supervisor (University of Exeter, UK) and advisor (Yale University, USA) July 2014.

SIR HARCOURT CAUGHEY AWARD – ($20,294 – 6 months) 7713001

Dr Rebecca Mairs
Dept of Psychiatry, Waitemata District Health Board

To undertake a 6 month Eating Disorders Fellowship at the Feeding and Eating Disorders Service (FEDS) at Great Ormond Street Hospital.

GAVIN AND ANN KELLAWAY MEDICAL RESEARCH FELLOWSHIP – ($12,943 – 3 months) 1513001

Dr Bruce Russell
School of Pharmacy, University of Auckland

To build on existing, and establish new, collaborations in the United Kingdom and USA and to attend conferences in Germany.

TRAVEL GRANTS AWARDED

Dr Marjan Askarian Amiri
Auckland Cancer Society Research Centre, University of Auckland

To attend The Non-Coding Genome meeting, Heidelberg, Germany, 9-12 October 2013

Dr Simon Backhouse
Dept of Optometry & Vision Science, University of Auckland

To attend the 14th International Myopic Conference, California, USA, 20-22 August 2013 and the 7th Annual Berkeley Conference on Translational Research Satellite Meeting, California, USA, 18-19 August 2013

A/Prof Joanne Barnes
School of Pharmacy, University of Auckland

To attend the 'Natural Products at a Crossroads: Current and Future Directions", American Society of Pharmacognosy Annual Meeting, Missouri, USA, 13-17 July 2013

Dr Christina Buchanan
Dept of Molecular Medicine & Pathology, University of Auckland

To attend the Annual Scientific Meeting of the Endocrine Society of Australia and the Society for Reproductive Biology 2013, 25-28 August 2013; Australian Diabetes Society & Australian Diabetes Educators Association Sydney, Australia, 28-30 August 2013

Dr Alys Clark
Auckland Bioengineering Institute, University of Auckland

To attend The American Thoracic Society (ATS) International Conference, Philadelphia, USA, 17-22 May 2013

Dr Nathan Consedine
Dept of Psychological Medicine, University of Auckland

To present aspects of research at the 27th Conference of the European Health Psychology Society, London, UK, 16-20 July 2013. Also to meet editorial board colleagues to conduct related symposia and attend collaborative meetings in UK.

Dr Theresa Davies
Mechanical Engineering, University of Auckland

To attend the Australasian Academy of Cerebral Palsy and Developmental Medicine Annual Conference, Hunter Valley, Australia, 10-15 March 2014

A/Prof Alan Davidson
Dept of Molecualr Medicine & Pathology, University of Auckland

To attend American Society of Nephrology Kidney Week 2013, Atlanta, USA, 5-10 November 2013

Dr Karen Falloon
Dept of General Practice & Primary Health Care, University of Auckland

To attend the Annual Scientific Conference of the Australasian Sleep Association, Brisbane, Australia, 17-19 October 2013

Dr Mhoyra Fraser
Liggins Institute & Dept of Physiology, University of Auckland

To attend the 40th Fetal & Neonatal Physiological Society (FNPS) Annual Meeting, Puerto Varas, Chile, 1-4 September 2013

Grants Awarded continued

Dr Robert Galinsky
Dept of Physiology, University of Auckland

To attend the 18th annual conference of The Perinatal Society of Australia and New Zealand (PSANZ), Perth, Australia, 6-9 April 2014

Dr Clint Gray
Liggins Institute, University of Auckland

To attend Endo 2013. The Endocrine Society's 95th, Annual Meeting & Expo, San Francisco, USA, 15-18 June 2013

Dr Angus Grey
Dept of Physiology, University of Auckland

To attend the International Conference on the Lens, Sheraton Kona Resort and Spa, Kona, Hawaii, 19-24 January 2014

Dr Natasha Grimsey
Centre for Brain Research, University of Auckland

To attend the Gordon Research Seminar in Molecular Pharmacology, the Gordon Research Conference in Molecular Pharmacology and to Visit the University of Zurich, Switzerland, 27 April-10 May 2013

Dr Joanna James
Dept of Obstetrics & Gynaecology, University of Auckland

To attend the Annual Scientific Meeting of the Endocrine Society of Australia and the Society for Reproductive Biology (SRB) Sydney, Australia, 25-28 August 2013 and The International Federation of Placenta Associations (IFPA) Meeting Whistler, Canada, 11-14 September 2013

Dr Jessica Jor
Auckland Bioengineering Institute, University of Auckland

To attend the 11th International Symposium Computer Methods in Biomechanics and Biomechanical Engineering (CMBBE), Utah, USA, 3-6 April 2013

Dr Maarten Koeners
Dept of Physiology, University of Auckland

To attend the Federation of American Societies for Experimental Biology (FASEB) Summer Research Conference 2013 - Renal Hemodynamics: Integrating with the nephron and beyond, Vermont, USA, 30 June – 5 July 2013; Invited talk and collaboration meeting at The Van Vliet Laboratory Memorial University of Newfoundland, Newfoundland, Canada, 5-9 July 2013

Dr Heidi Koschwanez
Dept of Psychological Medicine, University of Auckland

To attend the 72nd American Psychosomatic Society (APS) Annual Scientific Meeting, San Francisco, USA, 12-15 March 2014

A/Prof Geoffrey Krissansen
Dept of Molecular Medicine & Pathology, University of Auckland

To attend the 10th Australian Peptide Conference, Penang, Malaysia, 6-8 September 2013

Dr Jennifer Kruger
Auckland Bioengineering Institute, University of Auckland

To attend the 38th Annual Meeting of the International, Urogynaecological Association (IUGA), Dublin, Ireland, 28 May-1 June 2013

Dr Julie Lim
Dept of Optometry & Vision Science, University of Auckland

To attend The Association for Research in Vision & Ophthalmology, Seattle, USA, 5-9 May 2013

Dr Dong-Xu Liu
Liggins Institute, University of Auckland

To attend The 18th World Congress on Advances in Oncology & the 16th International Symposium on Molecular Medicine, Crete, Greece, 10-12 October 2013

Dr Mathijs Lucassen
Dept of Psychological Medicine, University of Auckland

To attend the European Society of Child and Adolescent Psychiatry (ESCAP) Congress, Dublin, Ireland, 6-10 July 2013

Mr Pau Medrano-Gracia
Dept of Anatomy with Radiology, University of Auckland

To attend the 16th International Conference on Medical Image Computing and Computer Assisted Intervention, Nagoya, Japan, 22-26 September 2013

Dr Kathy Mountjoy
Dept of Physiology, University of Auckland

To attend the Keystone Symposia joint Conferences: Obesity: A multisystems perspective (J2) and Challenges and opportunities in diabetes research and treatment, Vancouver, Canada, 12-17 January 2014

Dr David Musson
Dept of Medicine, University of Auckland

To attend the 50th European Calcified Tissue Society (ECTS) Annual Meeting, Lisbon, Portugal, 18-21 May 2013; International Conference on Tissue Engineering (ICTE), Leiria, Portugal, 6-8 June 2013

Dr Katrina Poppe
Dept of Medicine, University of Auckland

To attend the American Heart Association Scientific Sessions 2013, Texas, USA, 16-20 November 2013

Dr Shiva Reddy
Dept of Molecular Medicine & Pathology, University of Auckland

To attend the 6th Annual Meeting of the Network for Pancreatic Organ Donors with Diabetes (nPOD), Atlantic Beach, Florida, USA, 23-26 February 2014

Dr Clare Reynolds
Liggins Institute, University of Auckland

To attend The 95th Annual Meeting of the American Endocrine Society, San Francisco, USA, 15-18 June 2013

Dr Ilva Rupenthal
Dept of Ophthalmology, University of Auckland

To attend the European Association for Vision and Eye Research (EVER) 2013 Congress, Nice, France, 18-21 September 2013

Dr Bruce Russell
School of Pharmacy, University of Auckland

To attend the International Congress on Schizophrenia Research (ICSR) Orlando, USA, 21-25 April 2013

Dr Darren Svirskis
School of Pharmacy, University of Auckland

To attend the Controlled Release Society Annual Meeting & Exposition - Emerging Challenges for Global Delivery, Hawaii, USA, 21-24 July 2013; attending Young Scientist Workshop 20 July 2013

Dr Ruth Teh
Dept of General Practice & Primary Health Care, University of Auckland

To attend The 20th IAGG World Congress of Gerontology & Geriatrics, Seoul, Korea, 23-27 June 2013

Dr Mark Trew
Auckland Bioengineering Institute, University of Auckland

To attend Heart Rhythm 2013 (34th Annual Scientific Sessions of the Heart Rhythm Society), Denver, USA, 8-11 May 2013

Dr Stefanie Vandevijvere
Dept of Epidemiology & Biostatistics, University of Auckland

To attend the 12th International Congress on Obesity, Kuala Lumpur, Malaysia, 17-20 March 2014

Dr Tom Wang
Greenlane Cardiovascular Service, Auckland City Hospital

To attend the 61st Annual Scientific Meeting of the Cardiac Society of Australia and New Zealand (CSANZ) and 7th Annual Australia and New Zealand Endovascular Therapies Meeting (ANZET), Brisbane, Australia 7-11 August 2013

Dr Vicky Wang
Auckland Bioengineering Institute, University of Auckland

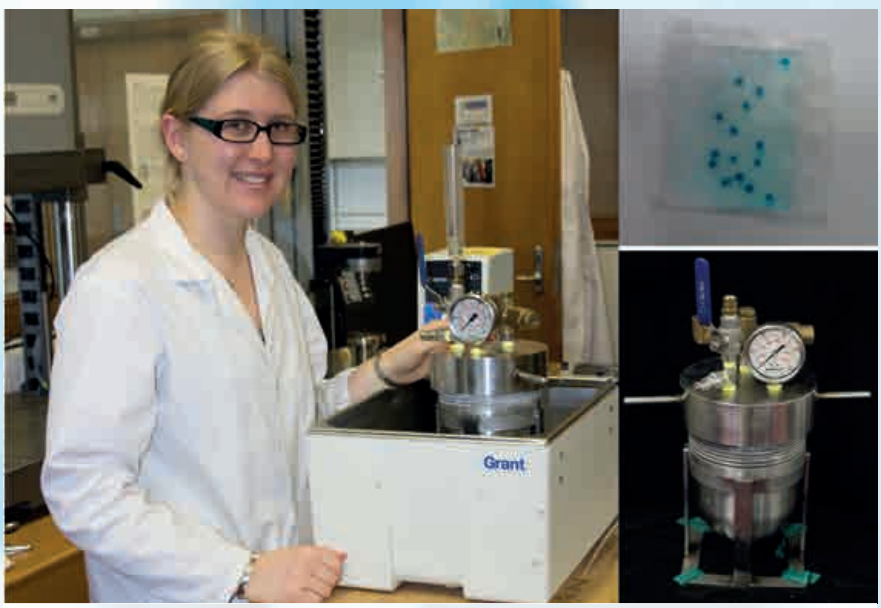
To attend the 7th International Conference on Functional Imaging and Modeling of the Heat (FIMH), London, UK, 20-22 June 2013

Dr Evelyn Sattlegger
Massey University, Albany

To attend European Molecular Biology Laboratory (EMBL), Heidelberg, Germany, 8-12 September 2013

Dr Jichao Zhao
Auckland Bioengineering Institute, University of Auckland

To attend The Heart Rhythm Society's 34th Annual Scientific Sessions, Denver, USA, 8-11 May 2013



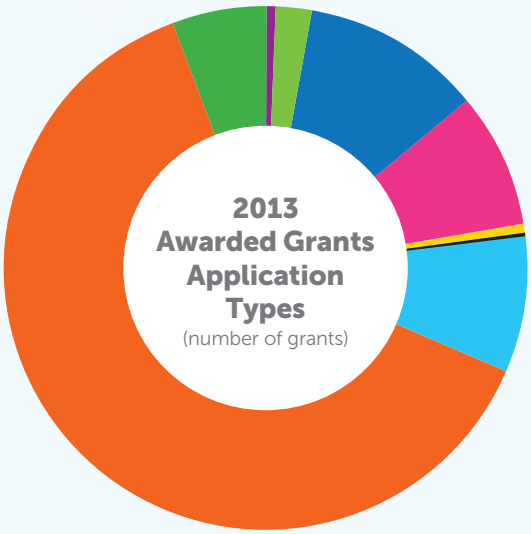
Ms Taryn Saggese next to her custom built hydrostatic pressure vessel. Taryn, an AMRF Doctoral Scholar, is in the final year of her PhD studies. Over the past 3 years, she has developed a model to study the role of chronic loads on cells of the intervertebral disc. Taryn will be presenting her findings in Lyon in October this year, at the Annual Conference of the Spine Society of Europe, Eurospine.

SUMMARY OF PROJECT IN PROGRESS

One in four adult New Zealanders suffer from chronic back pain. A major cause of back pain is degeneration of the intervertebral discs. Healthy discs contain a soft gel-like centre known as the nucleus pulposus, which help resist mechanical forces that are transmitted through the spine during daily movement. In degenerated discs, the nucleus pulposus becomes stiff and fibrous; this alters its mechanical properties and leads to disc failure and herniation, i.e. a slipped disc. While mechanical stress is a risk factor for disc degeneration, the underlying cause of the structural and cellular changes within the nucleus pulposus are poorly understood. Consequently there are no treatments available which are able to repair damaged discs. We believe that cells with the nucleus pulposus change behaviour in response to mechanical stress. This study aims to use isolated bovine nucleus pulposus cells to investigate the cellular changes which occur in response to mechanical stress. This study will use a custom built cell straining device to apply hydrostatic pressure to nucleus pulposus cells. The isolated and stressed cells will then be analysed for changes in cellular characteristics, gene expression levels and extracellular matrix production. Understanding the mechano-biological response of these cells will provide potential therapeutic targets for disc repair.

GRANTS IN PROGRESS

78 Grants Awarded Totalling $4,478,197



Ruth Spencer Medical Research Fellowship (1)	$257,333	5.7%
Sir Harcourt Caughey Award (1)	$20,294	0.5%
Travel grants (39)	$97,959	2.2%
Doctoral Scholarships (4)	$504,000	11.3%
Goodfellow Repatriation Fellowship (1)	$376,437	8.4%
Gavin and Ann Kellaway Medical Research Fellowship (1)	$12,943	0.3%
HealtheX Emerging Researcher Travel Award (1)	$5,000	0.1%
Postdoctoral Fellowships (2)	$382,640	8.5%
Project grants (28)	$2,821,591	63.0%

$ Value each theme % Total expenditure

Grants in Progress

EXOME SEQUENCING TO IDENTIFY THE CAUSES OF COMMON VARIABLE IMMUNE DEFICIENCY (2112017)

A/Prof Rohan Ameratunga, A/Prof Klaus Lehnert, Dr See-Tarn Woon, Dr Wikke Koopmans, Dr Anthony Jordan
Dept of Virology & Immunology, LabPLUS, Auckland City Hospital

FUNCTIONAL ROLE OF LONG NON-CODING RNAs IN HUMAN BREAST CANCER DEVELOPMENT (1111011)

Dr Marjan Askarian-Amiri, Dr Cherie Blenkiron, Professor Bruce Baguley
Auckland Cancer Society Research Centre, University of Auckland

IDENTIFICATION OF GENES INVOLVED IN TUMOUR-INDUCED LYMPHATIC GROWTH (1111015)

Dr Jonathan Astin, Prof Kathryn Crosier, Prof Phil Crosier
Dept of Molecular Medicine & Pathology, University of Auckland

PATHOPHYSIOLOGY AND NOVEL MANAGEMENT OF POSTOPERATIVE GASTROINTESTINAL DYSFUNCTION (1112012)

A/Prof Ian Bissett, Dr Ryash Vather
Dept of Surgery, University of Auckland

DOES WRITTEN EMOTIONAL DISCLOSURE IMPROVE WOUND HEALING IN SURGICAL PATIENTS? (1112013)

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

TRAFFICKING OF THE CREATINE IN LIVE NEURONS: DELIVERY OF CREATINE FOR MITOCHONDRIAL AND SYNAPTIC FUNCTION (1110002)

A/Prof David Christie
School of Biological Sciences, University of Auckland

PROTEOMIC AND IMAGING ANALYSIS OF GLYCOSYLATED PROTEINS IN HUMAN HEART FAILURE (1111009)

Dr David Crossman, Dr Mia Jullig, Dr Peter Ruygrok, A/Prof Christian Soeller
Dept of Physiology, University of Auckland

ROLE OF THE NOVEL PROTEIN PGAF IN RENAL DISEASE (1111001)

A/Prof Alan Davidson
Dept of Molecular Medicine & Pathology, University of Auckland

TARGETING EXTRACELLULAR MATRIX IN PRETERM BRAIN INJURY (1112002)

Dr Justin Dean
Dept of Physiology, University of Auckland

PROSPECTIVE EVALUATION OF OUTCOME IN PATIENTS WITH HEART FAILURE WITH A PRESERVED LEFT VENTRICULAR EJECTION FRACTION: The PEOPLE Study (1112010)

Prof Rob Doughty, Dr Maryana Lund
Dept of Medicine, University of Auckland

DURATION OF COLONISATION WITH EXTENDED-SPECTRUM BETA-LACTAMASE-PRODUCING ENTEROBACTERIACEAE (ESBLPE) (7112007)

Dr Dragana Drinkovic, Dr Hasan Bhally, Dr Susan Taylor, Dr David Holland, Dr Arlo Upton, Dr Simon Briggs
Microbiology Laboratory, North Shore Hospital

BIOMECHANICAL MODELLING TO EXPLAIN TOPHUS FORMATION AND BONE EROSION IN GOUT (1112008)

Dr Justin Fernandez, A/Prof Nicola Dalbeth, Dr Kumar Mithraratne
Auckland Bioengineering Institute, University of Auckland

MOLECULAR MECHANISMS OF CANNABINOID RECEPTOR 1 AND 2 INTRACELLULAR TRAFFICKING (1110018)

Dr Natasha Grimsey, A/Prof Michelle Glass
Centre for Brain Research, University of Auckland

VITAMIN D STATUS IN MĀORI AND NON-MĀORI PEOPLE OF ADVANCED AGE (1111017)

Prof Ngaire Kerse, Dr Catherine Bacon, Mr Avinesh Pillai, Dr Mark Bolland, Ms Karen Hayman, Dr Mere Kepa, Dr Lorna Dyall
Dept of General Practice & Primary Health Care, University of Auckland

PEPTIDE TECHNOLOGY TO COMBAT BREAST CANCER (1112003)

A/Prof Geoffrey Krissansen, Mr Glenn Bell, Ms Yi Yang
Dept of Molecular Medicine & Pathology, University of Auckland

TRIPLE NEGATIVE BREAST CANCER (1112006)

Dr Euphemia Leung, Prof Bruce Baguley
Auckland Cancer Society Research Centre, University of Auckland

CYSTEINE DELIVERY TO THE LENS (1112005)

Dr Julie Lim, Dr Angus Grey, Prof Paul Donaldson
Dept of Optometry & Vision Science, University of Auckland

THE SYNAPTIC BASIS OF HUNTINGTON'S DISEASE (1112018)

A/Prof Johanna Montgomery, Dr Ailsa McGregor
Dept of Physiology, University of Auckland

MELANOCORTIN TREATMENT FOR OBESITY (1112016)

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

THE A-PHIRST STUDY (AUSTRALASIAN PAEDIATRIC HEAD INJURY RULES STUDY): A PROSPECTIVE OBSERVATIONAL STUDY COMPARING EXISTING PAEDIATRIC MINOR HEAD INJURY CLINICAL DECISION RULES (3112011)

Dr Jocelyn Neutze
Kidz First, Middlemore Hospital

TARGETING THE HUMAN GROWTH HORMONE RECEPTOR IN ER+ BREAST CANCER (1112019)

Dr Jo Perry, Dr Dong-Xu Liu, Dr Stephen Jamieson, Prof William Wilson,
Liggins Institute, University of Auckland

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
National Women's Health, Auckland City Hospital

Wnt SIGNALING AS A LINK BETWEEN DIABETES AND ATHEROSCLEROSIS (1112015)

Prof Peter Shepherd, Dr Brie Sorrenson
Dept of Molecular Medicine and Pathology, University of Auckland

HEALING WITH HOLOCLONES (1111010)

A/Prof Trevor Sherwin
Dept of Ophthalmology, University of Auckland

OTOPROTECTION BY ADENOSINE RECEPTORS (1112009)

A/Prof Srdjan Vlajkovic, Prof Peter Thorne, Dr Detlev Boison, Prof Gary Housley
Dept of Physiology, University of Auckland

P2 RECEPTOR SIGNALLING IN THE COCHLEA SUPPORTS HAIR CELL SURVIVAL UNDER STRESS (1110013)

A/Prof Srdjan Vlajkovic, Prof Peter Thorne, Prof Gary Housley
Dept of Physiology, University of Auckland

IMPROVING SAFETY FOR SURGICAL PATIENTS: A MULTIDISCIPLINARY, SIMULATION-BASED INTERVENTION TO IMPROVE COLLABORATION AND INFORMATION SHARING IN THE OPERATING THEATRE (1112014)

A/Prof Jennifer Weller, Prof Alan Merry, Mr Ian Civil, Ms Wendy Guthrie, Dr Craig Webster, Dr Jane Torrie, Mr Andrew MacCormick, Dr David Cumin, Dr Matt Boyd
Dept of Anaesthesia, University of Auckland

THE CLINICAL UTILITY OF SPUTUM PROCALCITONIN, A NOVEL MARKER OF BACTERIAL INFECTION, IN BRONCHIECTASIS (3110015)

Dr Conroy Wong, Dr Sarah Mooney, Dr Susan Taylor, Dr Lata Jayaram, Dr David Holland, Dr Stuart Jones, Dr Irene Zeng
Dept of Medicine, Middlemore Hospital

THE DEVELOPMENT OF EXECUTIVE FUNCTION IN CHILDREN EXPOSED PRENATALLY TO METHAMPHETAMINE, "P" (1112004)

Dr Trecia Wouldes, Dr Linda Lagasse, Dr Barry Lester
Dept of Psychological Medicine, University of Auckland

INTELLIGENT ROBOT ASSISTED GAIT REHABILITATION SYSTEM (1111014)

Prof Xhane Xie, Dr John Parsons
Dept of Mechanical Engineering, University of Auckland

MAPPING STUDY OF PERSISTENT ATRIAL FIBRILLATION (1112020)

Dr Jichao Zhao, Prof Bruce Smaill, Dr Nigel Lever
Auckland Bioengineering Institute, University of Auckland

NAMED FELLOWSHIPS

POSTDOCTORAL FELLOWSHIPS

ARE GENERIC MEDICINES ACTUALLY LESS EFFECTIVE AND MORE LIKELY TO CAUSE SIDE EFFECTS, OR DO WE JUST BELIEVE THAT THEY ARE? (1312001)

Dr Kate Faasse
Dept of Psychological Medicine, University of Auckland

DISCOVERING BIOMARKERS FOR TREATMENT RESISTANCE IN PEOPLE WITH SCHIZOPHRENIA (1311001)

Dr Valerie Anderson
School of Pharmacy, University of Auckland

FROM MICROTUBULES TO COMPLEX NEURONS: HOW DOES NEUROSERPIN SIGNAL THE MICROTUBULE NETWORK TO REGULATE NEURONAL DEVELOPMENT (1310002)

Dr Tet Woo Lee
School of Biological Sciences, University of Auckland

EVALUATION OF SCAFFOLD MATERIALS FOR TENDON REGENERATION (1311002)

Dr David Musson
Dept of Medicine, University of Auckland

Grants in Progress continued

DOCTORAL SCHOLARSHIPS

BRIAN DE LUEN DOCTORAL FELLOWSHIP

THE REGULATION OF STEM CELL MIGRATION IN PARKINSON'S DISEASE (1210001)

Miss Sheryl Tan
Centre for Brain Research, University of Auckland

USING FUNCTIONAL AND STRUCTURAL MRI TO EXPLORE PLASTICITY IN THE HUMAN VISUAL CORTEX (2110044)

Mr Victor Borges
Dept of Optometry and Vision Science, University of Auckland

GLUTAMATE AND ITS *N*-METHYL-D-ASPARTATE RECEPTORS (NMDARS) IN HUMAN MELANOMA (1211001)

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

GENETIC VARIANTS AND SUDDEN CARDIAC DEATH SYNDROMES (1211002)

Miss Nicola Earle
Dept of Medicine, University of Auckland

DEVELOPMENT OF BIOMARKERS FOR IMPROVED EMBRYO SELECTION IN IVF (1212001)

Miss Elizabeth Hammond
Dept of Obstetrics and Gynaecology, University of Auckland

THE EFFECT OF NEONATAL HYPOGLYCAEMIA ON VISUAL DEVELOPMENT (1212002)

Mr Nabin Paudel
Dept of Optometry & Vision Science, University of Auckland

MECHANOBIOLOGY OF THE NUCLEUS PULPOSUS; THE ROLE OF NOTOCHORDAL CELLS IN INTERVERTEBRAL DISC DEGENERATION (1210002)

Miss Taryn Saggese
Dept of Anatomy with Radiology, University of Auckland

CHARACTERISATION OF LIVER ANTIGEN PRESENTING CELLS (1212003)

Dr Otto Strauss
Dept of Surgery, University of Auckland

COCHLEAR INFLAMMATION: MECHANISMS AND THERAPIES (1209003)

Mr Winston Tan
Dept of Physiology, University of Auckland

CAN HUMAN AMNIOTIC EPITHELIAL CELLS REPAIR THE INJURED PRETERM BRAIN? (1211003)

Miss Lotte Van Den Heuij
Dept of Physiology, University of Auckland

OTHER GRANTS

SIR HARCOURT CAUGHEY AWARD

FUNDING FOR VISITING ACADEMIC PROFESSOR CHRISTINA PUCHALSKI, DIRECTOR OF THE GEORGE WASHINGTON INSTITUTE FOR SPIRITUALITY AND HEALTH, UNIVERSITY OF WASHINGTON (1712001)

Dr Peter Huggard
Dept of General Practice & Primary Health Care, University of Auckland

GLOW WORM ANIMATION OUTREACH PROJECT (6712002)

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

An AMRF Success Story

IMPROVING THE BODY'S ABILITY TO HEAL ITSELF – BY PROFESSOR COLIN GREEN

Professor Colin Green.

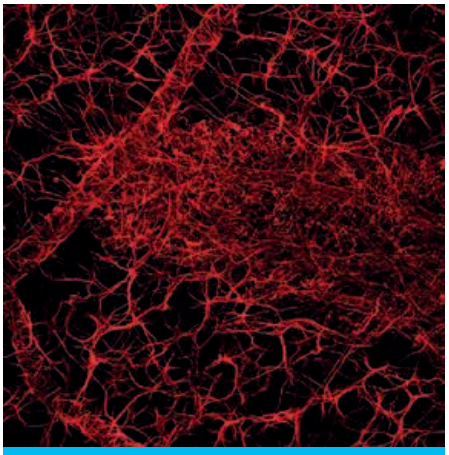
Faster wound healing with reduced scarring and improved functional outcome is a desirable health research target. Of more concern though are chronic or non-healing wounds which impose upon quality of life and have significant cost and healthcare ramifications. Venous leg ulcers in the United States alone account for two million working days a year lost and three billion dollars annually in treatment costs. Approximately 15% of diabetics will develop foot ulcers during their lifetime, and more than 2.5 million people each year in the United States develop pressure ulcers (figures for New Zealand are less robust but we are likely to have similar incidence rates). Globally, 43,000 deaths resulted from pressure ulcers in 2010. Treatment of these ulcers and related injuries, including to the eye, has remained difficult.

Direct cell-to-cell communication through structures called gap junctions, and uncontrolled opening in the cell membrane of the undocked half channels that make up gap junctions, has been shown to lead to wound lesion spread, inflammation and scarring. Professor Green and his team at the University of Auckland, working with colleagues at University College London, developed a gel containing short single stranded antisense DNA to transiently down regulate the expression of the gap junction protein in wounds. It has been shown in multiple models that this reduces lesion spread, reduces swelling and inflammation and can double the rate of healing. In particular, it triggers healing in wounds that have otherwise stalled. The first human to be treated with this technology was an Auckland patient with a severe chemical burn to the eye which was not healing. A single treatment with the drug triggered healing and saved the man's sight. The research led to the establishment of CoDaTherapeutics (NZ) Ltd and subsequently CoDa Therapeutics, Inc. in the United States. The company has now successfully completed phase two clinical trials for both venous and diabetic leg ulcers and the drug has possible application in many wound healing areas.

Professor Green and colleagues then set out to develop a second blocker which could be delivered through the blood stream in order to treat internal lesions such as spinal cord injury and stroke. This channel regulator is a peptide that also targets a common sign of injury and inflammation; gap junction channel mediated vascular haemorrhage. Because of this, it has potential to alleviate several chronic inflammatory diseases such as age related macular degeneration, diabetic retinopathy, arthritis and neurodegenerative diseases such as Alzheimer's and Parkinson's which all share a microvascular dropout component. This second blocker has so far proven to be effective in retinal stroke (effectively a two dimensional form of brain stroke), perinatal ischaemia and spinal cord injury models.

Q1. Please can you tell us a bit about yourself and how you came to be in this area of research?

I did my PhD at the University of Auckland and then worked overseas for twelve years in France, England and the United States. During that time I was in London for more than eight years, the last seven as a Royal Society University Research Fellow and Reader at University College London. My research there focused on cardiac gap junctions and developmental biology. I returned to Auckland in 1993 and in parallel with cardiac research developed the antisense approach to study gap



Astrocytes in the retina labelled for GFAP are seen to wrap around two blood capillaries on the left. The retina was made ischaemic for one hour and this image taken four hours later shows an area of astrocytosis (a sign of inflammation) correlating with gap junction hemichannel mediated vascular leak.

junction roles in limb patterning. Fortuitously I had a student who insisted on working on the brain and we tested the hypothesis that blocking gap junction channels would make a lesion worse. The result was the opposite and it was downhill from there. At that time I was in Anatomy with Radiology and in 2005 I moved to Ophthalmology. We still do a lot of work on the central nervous system, especially spinal cord and in the retina of course, but the drug development was primarily on surface wounds to the skin and cornea of the eye.

Q2. How has AMRF funding allowed your research to evolve or progress to the next stage?

AMRF funding played a crucial role in the establishment of my research laboratory upon returning to Auckland. I was able to bring some equipment from London with me, but getting a new laboratory up and running is a big task. My first AMRF grant in 1993 was to continue my cardiac gap junction work. That grant was instrumental in provisioning the laboratory and in establishing a research team in Auckland. At that time I was Director of the newly established Biomedical Imaging Research

continued overleaf

An AMRF Success Story continued from previous page

IMPROVING THE BODY'S ABILITY TO HEAL ITSELF – BY PROFESSOR COLIN GREEN

Unit which also had AMRF funding towards the purchase of Auckland University's first confocal laser scanning microscope. That instrument was incredibly important in the research of many university and external groups. In 2004 we obtained an AMRF grant to look at scar formation in the skin, and in 2006 an AMRF grant to use the antisense approach for glaucoma flap surgery. The AMRF funded research led not only to high impact publications but also seeded projects that went on to attract other funding and support, and ultimately to the translational research pathway and novel drug developments.

Q3. Please can you tell us a bit about how your research outcomes are being used in New Zealand, and the benefit to New Zealanders from your research:

Since returning to Auckland my research has supported over 50 postgraduate students, almost all of whom have gone on to develop their own careers academically or in business. Several have completed medicine or become clinical specialists (particularly in Ophthalmology). With the drug development we were able to treat (and heal) five non healing eye burns in New Zealand before the drug entered full clinical trials, with New Zealand the primary clinical site for CoDa Therapeutics first five trials. The company employs most of its staff in New Zealand, providing not only jobs, but further expanding New Zealand's capability and expertise in drug development. CoDa Therapeutics Inc. brought in $90M of international investment whilst I was on the Board of Directors with a good proportion of that spent in New Zealand. New Zealand retains some intellectual property rights.

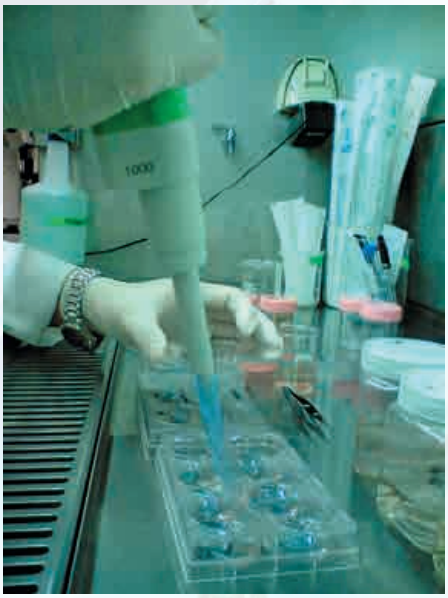
Longer term our research base continues to grow and over the last ten years a move towards more outcome focused research has become more acceptable. Our own research has revealed three further translational opportunities and we are working with Auckland UniServices Ltd on those. These have potential to provide further economic opportunities for New Zealand, but more importantly, improvements in health care for all New Zealanders.

Q4. Have there been significant overseas breakthroughs or collaborations resulting from your research? Please can you describe your team's contribution to the global research effort in your area:

We have international research collaborations in the United States, Australia, Scandinavia, China, South America and Europe, and our work has raised awareness of gap junction roles in many wound healing and disease processes. Three other companies in France, Denmark and the United States have followed and complement CoDa's approach to gap junction channel regulation. In the past 5 years we have published 45 full research papers and book chapters, and in the past two years I have been a keynote speaker at conferences in Australia, Singapore, Chile, Belgium, China and the United States. My collaborators and team members have also presented our work throughout the world.

Q5. What is the next step in your research plan?

We will continue to research gap junction channel roles in perinatal ischaemia and infection, for diseases of the eye such as glaucoma, age related macular degeneration and diabetic retinopathy, and central nervous system injury, in particular spinal cord injury. The most exciting new area arises from analysis of our acute and chronic wound models which has led us to hypothesise that in cancer it may not be growth of new vessels that promotes tumour expansion as has been the conventional belief for the past 40 years, but rather vascular haemorrhage and disruption as a result of the inflammatory tumour environment into which vessels are



growing. Protection of blood flow should reduce tumour hypoxia, promote survival of normal cells, enable the body's immune system to better respond to the tumour, enable improved delivery of cytotoxic drugs or anti-tumour cells, and increase the effectiveness of radiation therapy. This work has attracted Return on Science funding and enabled new collaborations with Cancer Research and colleagues in Melbourne. The initial results are most encouraging.

Q6. What is your greatest hope or dream for research in this field?

To see a New Zealand discovered drug go from the basic research stage to treatment of disease. In our case, the opportunity to improve the lives of so many is a very significant driver. The pleasure in seeing something arising from basic research in your own laboratory being used to save a person's sight as we have done is indescribable. To see such a drug available for all, with its multiple indications from leg ulcers to persistent epithelial defects in the eye, is my dream.

GRANTS COMPLETED

78 Grants Awarded Totalling $4,478,197

Clinical (15) | $666,924 14.9%

Population Health (5) | $295,064 6.6%

Biomedical (58) | $3,516,209 78.5%

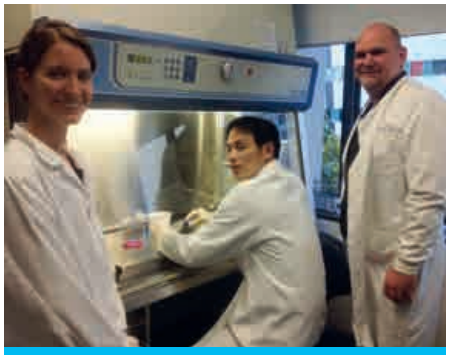
$ Value each theme % Total expenditure

Grants Completed

PROJECTS

NECROTIC SYNCYTIAL KNOTS IN PREECLAMPSIA (1110020)

Prof Larry Chamley, Dr Qi Chen, Prof Peter Stone
Dept of Obstetrics & Gynaecology, University of Auckland



A/Prof Larry Chamley (Right), Dr Qi Chen (Centre) with PhD student Chez Viall (Left).

Preeclampsia affects approximately 3,000 New Zealand women and their babies annually. Preeclampsia causes potentially life-threatening high blood pressure in pregnant women and often requires the delivery of the baby, before it is due, to prevent the death of the mother or baby. It is known that something from the placenta triggers preeclampsia but not exactly what this is. We have increasing evidence that dead cells from the placenta called syncytial knots may be this trigger. The way in which the syncytial knots die probably affects whether a pregnancy will be affected by preeclampsia. We had previously found preliminary evidence that autoantibodies called antiphospholipid antibodies, which are found in some women with a high risk of developing preeclampsia, caused aberrant death of syncytial knots such that they might induce preeclampsia. In this research we have confirmed that antiphospholipid antibodies from affected women do cause aberrant cell death in the syncytial knots and have begun to investigate the mechanism by which the antibodies do this so that we can identify a way to treat women with antiphospholipid antibodies to prevent them developing preeclampsia.

OPTIMISING A NOVEL INDUCED NEURAL PRECURSOR-LIKE CELL LINE (1111004)

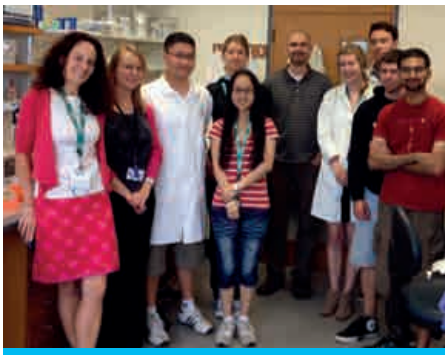
A/Prof Bronwen Connor
Dept of Pharmacology, Centre for Brain Research, University of Auckland

A/Prof Bronwen Connor in her Lab.

Recent advances in stem cell biology have shown that mature cells, such as skin cells, can be transformed back to an "embryonic-like" stem cell state where cells exhibit pluripotency (the ability to become any cell type) by the expression of specific genes. Advancing this, the current project has demonstrated that we can use two genes to generate immature brain cells (neural precursor cells) directly from adult human skin without the need to first generate an intermediate embryonic stem cell. From these neural precursor cells we can produce mature brain cells. This technology can be used to "model" neurological diseases by obtaining skin cells from patients with specific neurological disorders and generating neural precursor cells, and subsequently generate mature brain cells to study the disease process in human brain cells and potentially identify novel therapeutic target.

ISOLATION OF RENAL STEM CELLS (1112001)

A/Prof Alan Davidson, Dr Teresa Holm, Ms Aneta Przepiorski
Dept of Molecular Medicine & Pathology, University of Auckland



A/Prof Davidson (centre) with staff and students from his Lab.

New Zealand has an alarmingly high rate of kidney disease and there is an urgent need to find better therapies. Regenerative medicine utilising tissue-specific stem cells offers the potential to treat a wide range of chronic illnesses. In this study we initially set out to coax pluripotent stem cells, with the potential to form all 200 cell types in the body, to mature into kidney stem cells with the ultimate goal of using these cells to develop new renal therapies. In the process, we discovered a method for generating a particular type of kidney cell called the proximal tubule epithelial cell, which is damaged in patients with acute kidney injury. Being able to produce limitless numbers of proximal tubule cells will advance efforts to develop bioartificial kidneys and will be a valuable tool to search for drugs that prevent kidney damage or speed up repair after injury.

PREDICTING RISK OF END STAGE RENAL DISEASE IN DIABETES (1110019)

A/Prof C Raina Elley, A/Prof Tim Kenealy, Dr John Collins, Dr Paul Drury, Mrs Elizabeth Robinson, Dr Tom Robinson
Dept General Practice and Primary Health Care, University of Auckland

A/Prof Raina Elley.

There is an epidemic of type 2 diabetes in New Zealand; a major complication in this population is kidney disease, which can lead to kidney failure, dialysis and early death. Besides the large human cost of diabetic kidney disease, there are significant economic costs to the health system and community. Numbers of people on dialysis have been rising steadily over the past two decades. If effective treatment (particular blood pressure lowering medications and better glycaemic control) could be started at an early stage in people at highest risk, rates of progression to kidney failure could be slowed, producing considerable savings both in terms of quality of life and costs to the health service. This study developed and validated a 'renal risk score' that can be used to assess an individual's risk of progressing to kidney failure based on a number of risk factors. The risk score was very accurate at predicting risk and performed better than other international renal risk scores in the NZ population. The results of the study are about to be published in the international journal Diabetes Care.

DIABETES CVD RISK EQUATION VALIDATION (1111003)

A/Prof C Raina Elley, A/Prof Tim Kenealy, Dr Tom Robinson, Dr Paul Drury, Prof Bruce Arroll, Dr Sue Wells
Dept General Practice and Primary Health Care, University of Auckland

A/Prof Raina Elley with the team (Back row: Dale Bramley, Simon Moyes, Paul Drury, Bruce Arroll, Tim Kenealy; Front row: Elizabeth Robinson, Raina Elley, Ngaire Kerse).

People with diabetes are at increased risk of having a heart attack or stroke. This risk can be calculated for each person, depending on their demographic and health characteristics, and used to help decide on the best treatment. Current risk calculation, however, is based on findings from a US study conducted more than 50 years ago. We have developed and validated a new risk equation, using recent New Zealand data. The new equation suggests that we are currently under-treating certain groups in New Zealand, including people with poorly controlled diabetes or kidney impairment, especially for Māori, Pacific and Indian populations. The new NZ equation can now be used by clinicians to calculate patients' cardiovascular risk http://www.nzssd.org.nz/cvd/ on the website of the New Zealand Society for the Study of Diabetes (NZSSD).

A 'DARTMOUTH' ATLAS OF VASCULAR DISEASE FOR THE AUCKLAND REGION (1110022)

Dr Daniel Exeter, Dr Susan Wells, Prof Rod Jackson, Dr Tania Riddell, Dr Cam Kyle
Dept of Epidemiology & Biostatistics, University of Auckland

Dr Daniel Exeter at his work station.

Variation in health care delivery and patient outcomes are often best described pictorially which renders complex data into a form that is accessible for consumers, clinicians and policy makers alike. Our project integrated methods from epidemiology and geography to investigate and map the provision of cardiovascular disease (CVD) services (community laboratory tests, pharmaceutical management and hospital procedures) and the burden of CVD and diabetes for the Auckland Region. These analyses were possible because of the improved quality of routinely collected health databases in New Zealand, enabling an individual's anonymised health service records to be linked. All maps we developed during this project are now publically available on the internet with user-friendly guides and commentary to help navigation and understanding. We found substantial variations in the occurrence of diabetes and CVD, in addition to variations in medication dispensing and the proportion of the population having cholesterol (lipid) tests. This research, which will be discussed with regional health service providers, has significance for the evaluation of equity and where targeted improvement efforts are required to lift the quality of health service provision for population groups within the Auckland Region. It has particular significance for Māori, Pacific and Indian peoples who suffer disproportionately from the burden of vascular diseases.

Grants Completed continued

ENDOCANNABINOID MODULATION OF DOPAMINERGIC NEURONS IN THE SUBSTANTIA NIGRA – FUNCTION IN HEALTH AND IMPLICATIONS FOR DISEASE (1310001)

Dr Peter Freestone
Dept of Physiology & Centre for Brain Research, University of Auckland

Dr Peter Freestone.

Endocannabinoids are chemicals produced in the brain where they, amongst other things, fine tune the communication between brain cells. My research has uncovered a novel process whereby endocannabinoids control the activity of brain cells in an important brain region called the Substantia Nigra pars compacta (SNc). Brain cells in the SNc gradually die off giving rise to Parkinson's disease – a movement disorder affecting 1 in 500 New Zealanders. The role of endocannabinoids in the SNc allows brain cells to switch between active and less active states. How this relates to Parkinson's disease symptoms is still the topic of further investigation. In addition, we found that a unique endocannabinoid called NADA mediates this effect. The therapeutic potential of targeting endocannabinoid functions is gaining interest and is the subject of intense international research for many diseases. The novel mechanism discovered here highlights the potential of targeting endocannabinoid function in the SNc in the treatment of Parkinson's disease and other similar disorders.

ARE CANNABINOID CB2 RECEPTORS IN THE HUMAN BRAIN? (1111007)

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

A/Prof Michelle Glass, Scott Graham and Christa McDonald looking at some in situ hybridisation results.

Cannabinoid CB2 receptors have been suggested to be an appealing target for neuroinflammatory disorders, as many believe them to be found only on immune cells. However, their distribution is actually highly controversial with some groups reporting widespread neuronal distribution, while others see little evidence for CB2 in the brain. Part of the reason for these discrepancies is that the antibodies used to detect this protein are not entirely specific. Furthermore, many of the assumptions about CB2 expression in the brain are based on animal studies and may not represent the situation in the human brain. As many drug companies are aiming to bring CB2 directed therapies onto the market it is critical that the localisation of the receptor be accurately determined. In this project we have developed a sensitive method for determining the expression of CB2 in the normal healthy brain, while our current progress is suggesting that there is not CB2 in the normal human brain, we still need to do a few more experiments to confirm this finding.

PREVENTING ATOPY WITH VITAMIN D (1111019)

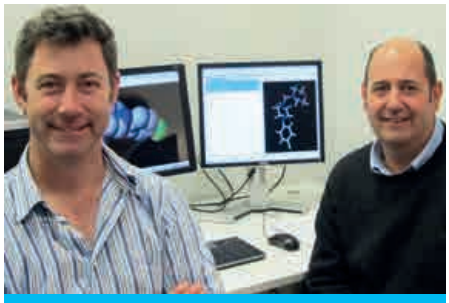
A/Prof Cameron Grant, Dr Clare Wall, Prof Ed Mitchell, Mr Alistair Stewart, Prof Carlos Camargo, Prof Robert Scragg, Prof Julian Crane, Dr Alec Ekeroma, Dr Sue Crengle, Dr Adrian Trenholme, Dr Jan Sinclair
Dept of Paediatrics: Child & Youth Health, University of Auckland

A/Prof Grant Cameron.

Vitamin D deficiency is recognised as a prevalent public health issue. Pregnant women and young children are age groups at increased risk. In this randomised, placebo-controlled clinical trial we have shown that vitamin D deficiency during early infancy can be prevented with daily vitamin D supplementation which starts during pregnancy. Our study indicates that a higher dose of vitamin D than is currently recommended is likely to be necessary in order to sustain adequate vitamin D status during infancy. An indication that this higher dose is associated with improved health is evident from our review of the primary care records of these children. In comparison with those infants randomised to placebo, a smaller proportion of infants in the higher dose vitamin D group made a GP visit for an acute respiratory infection in the first year of life. We are continuing to follow these children to determine if vitamin D supplementation can also prevent the development of the atopic state which is a precursor to eczema, food allergy and asthma.

DESIGN AND SYNTHESIS OF NOVEL ADRENOMEDULLIN-1 RECEPTOR ANTAGONISTS AS POTENTIAL ANTI-TUMOUR AGENTS (1111005)

A/Prof Michael Hay, A/Prof Debbie Hay, Dr Jack Flanagan
Auckland Cancer Society Research Centre, University of Auckland



A/Prof Michael Hay (right) with Dr Jack Flanagan (left).

One of the hallmarks of cancer is increased formation of blood vessels (angiogenesis) and this process is mediated, in part, by a hormone known as adrenomedullin (AM). AM acts to stimulate signalling and promote blood vessel growth through the AM receptor which is found on the surface of cells. The receptor is made of two subunits; between these is a groove, where AM binds to produce its effects. We have used medicinal chemistry, combined with molecular modelling, to create new molecules that block access of AM to this groove and hinder its ability to signal through the AM receptor. We have demonstrated that an example of this class can reduce the formation of lymph vessels in a zebra fish model. We continue to develop these molecules and improve their potency and selectivity for the AM receptor. These new agents will be useful to define the role of AM signalling in the formation of new blood and lymph vessels and may be the basis of new anti-angiogenesis agents for the treatment of cancer.

DOES PACIFIER USE REDUCE THE RISK OF UPPER AIRWAYS OBSTRUCTION IN INFANTS? (1109017)

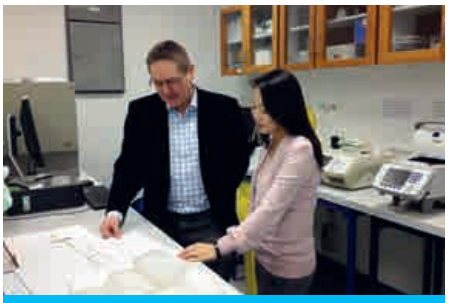
Dr Christine McIntosh, Dr Shirley Tonkin, Prof Alistair Gunn
Dept of Physiology, University of Auckland

Dr Christine McIntosh.

We sought to discover the reason why Sudden Unexpected Death in Infancy (SUDI) is less likely to occur when an infant has used a pacifier (dummy) during the last sleep. Our previous research on infants in car seats showed that when a baby's lower jaw is pushed back and upwards, the tongue inside the jaw can narrow or block the baby's airway. Conversely we have shown that babies' lower jaws come forward when they use a pacifier during sleep. The results of this study suggest that sleep using a pacifier may improve airway size and oxygenation in infants who were already used to sucking on a pacifier. However, of concern we found that infants who had not used a pacifier before were reluctant to suck on the pacifier and appeared to show a small reduction in mean oxygenation and airway size for the (much shorter) time that they had with the pacifier. Whilst pacifiers have been associated with reduced risk of SUDI, offering one to all infants is not the answer. Studying infants who are using pacifiers will add to our understanding of how babies control their upper airway and what causes SUDI.

CALCIUM AND MAGNESIUM INFUSIONS FOR OXALIPLATIN NEUROTOXICITY (1110014)

A/Prof Mark McKeage
Dept of Pharmacology and Clinical Pharmacology, University of Auckland



A/Prof Mark McKeage and Dr Catherine Han discuss results.

An intervention to counter the neurotoxic effects of a chemotherapy treatment for cancer has been withdrawn after AMRF-supported research showed it was ineffective. This resulted in big savings in the cost of the intervention and in treatment time by nurses, at Auckland City Hospital's medical oncology service. The neurotoxic effects of oxaliplatin chemotherapy treatment for patients can include acute effects such as excruciating pins and needles, muscle spasms, throat tightness and blurred vision. For some patients these neuro-symptoms can persist and many patients develop chronic neurotoxicity resulting in numbness in their fingers and toes for months or years after discontinuation of oxaliplatin chemotherapy. Auckland's medical oncology service did about 1,200 oxaliplatin infusions in the past year. The AMRF-supported research into the effectiveness of the calcium and magnesium infusions given to cancer patients to counter the neurotoxic effects of chemotherapy treatment with oxaliplatin clearly showed it was not working. On the basis of this new evidence, the calcium/magnesium intervention was withdrawn. It has led to a change in clinical practice in our cancer treatment centre at Auckland Hospital but also saved more than $17,000 each year as well as about 800 hours of nursing time.

Grants Completed continued

3T MRI TO ASSESS THE PROGRESSION OF CARTILAGE DAMAGE IN RHEUMATOID ARTHRITIS; A PROSPECTIVE 4 YEAR FOLLOW-UP STUDY (1111018)

Prof Fiona McQueen, A/Prof Nicola Dalbeth, A/Prof Anthony Doyle, Mr Quentin Reeves
Dept of Molecular Medicine & Pathology, University of Auckland

Prof Fiona McQueen.

Magnetic Resonance Imaging (MRI) scanning is a new form of imaging that can be very helpful to assess the inflammation and damage occurring inside the joints in patients with rheumatoid arthritis. Our group has been involved in this area of research for the last 18 years and we have learned much over this period about the way these scans can be used. This project investigated cartilage inside joints of the wrist in rheumatoid arthritis patients. On MRI scans, cartilage appears as a thin layer of tissue which covers the surfaces of the bones. Damage to cartilage is represented as further thinning of this layer. We are able to score damage to this cartilage layer using a scoring system developed by our group 3 years ago. The current project has shown that cartilage damage progresses over a 3 year period. Those patients with the worst damage at baseline were the same patients who sustained further damage to cartilage. There was also an association between more severe joint inflammation (especially affecting bone) and progression of cartilage damage. These findings help point the way towards using MRI in rheumatoid arthritis patients, aiming for better management and less joint damage in the long term.

CUTTING PROTEINS NOT CALORIES TO MAKE FAT MICE THIN (1110003)

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

Dr Kathy Mountjoy (Left) Dr C Buchanan (centre) Dr Ailsa McGregor (right).

Stress, weight gain and glucose metabolism are influenced by a group of hormones called melanocortins. The melanocortin family of hormones is derived from one large precursor protein known as pro-opiomelanocortin (POMC) found in the brain and periphery. Special enzymes chop-up POMC to form multiple melanocortin hormones, according to the body's requirement. To study what effects different melanocortins have on physiological function, we developed a mouse that lacks two melanocortins known as desacety -melanocyte stimulating (des- -MSH) hormone and -melanocyte stimulating hormone (-MSH). We characterised the effects of a lack of these melanocortins on weight gain. Mice lacking des-MSH and -MSH did not appear to differ from wild type (normal) mice until puberty when mice started to gain more weight than wild type mice. The weight gain was associated with increased body fat. To confirm that the obesity was due to a lack of these two melanocortins, we added back either des-MSH or -MSH into the brain or peripherally. Treatment of obese adult mice lacking both melanocortins with either des--MSH or -MSH into the brain significantly reversed the obesity. Peripheral administration of -MSH, but not des-MSH, also significantly reduced body weight. It is widely assumed that central -MSH is the main melanocortin regulating fat mass. Our data is the first to establish that (1) central des--MSH is also a potent regulator of body fat and (2) peripheral -MSH can regulate mouse body weight. A better understanding of the function of these two hormones could aid in future development of improved tests and treatments for disorders such as obesity.

PILVAX - A NOVEL PEPTIDE DELIVERING SYSTEM? (1111016)

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

Streptococcus pyogenes (group A streptococcus, GAS) is a human pathogen that causes diseases, ranging from pharyngitis, tonsillitis and skin diseases to life-threatening conditions such as necrotising fasciitis ("flesh eating disease") and streptococcal toxic shock syndrome (STSS), and serious post-streptococcal diseases, like acute rheumatic fever (ARF). The aim of our project was to use the streptococcal pilus structure, a hair-like protrusion from the bacterial cell surface, as a peptide delivery vehicle in vaccinations. *Lactococcus lactis*, a harmless relative of GAS, was genetically engineered to express the GAS pilus on the cell surface. Each pilus is made up of repeating protein subunits that are assembled by the bacteria to form the hair-like fibre. Consequently, introduction of a peptide into the subunit will result in many copies of the peptide on the cell surface, which should improve the immune response against the peptide. Although we achieved strong immune responses against the pilus proteins, no significant response to the model peptide OVA 323-339 could be achieved. We believe this is due to proteolytic degradation of the peptide after vaccination and we are currently generating four alternative constructs with the peptide inserted at different locations within the subunit protein.

THERAPEUTIC POTENTIAL OF S. AUREUS VIRULENCE FACTORS IN INFLAMMATORY (1110017)

Dr Fiona Radcliff, Dr Hyun-Sun Jin, Prof John Fraser
Dept of Molecular Medicine & Pathology, University of Auckland

Dr Fiona Radcliff in her laboratory

Staphylococcus aureus produces a range of molecules that interfere with the development of effective immune function. Staphylococcal Superantigen-Like protein 7 (SSL7) is a very well characterised molecule that inhibits Complement C5, a key component of the inflammatory response. We have successfully demonstrated that treatment with SSL7 can reduce inflammation in models of Inflammatory Bowel Disease and Allergic Airways Disease. The results we have generated will help us design future treatment strategies based on SSL7 and also provide new information on the role of C5 in inflammatory disease.

PROBING THE ACTIVE SITE OF AKR1C3 (1110004)

Dr Christopher Squire, Dr Jack Flanagan
School of Biological Sciences, University of Auckland

Dr Christopher Squire and Miss Yuliana Yosaatmadja operating the X-ray diffraction equipment.

We aimed to characterise the AKR1C3 enzyme active site to design a better analogue of the hypoxia-activated prodrug PR-104A, which reached stage II clinical trials but showed toxicity associated with binding the protein AKR1C3. Over the two year grant period we produced ~30 crystal structures of AKR1C3 incorporating different molecules in the active site e.g. NSAIDs, fragments for drug discovery (having first completed a 500 condition fragment screen), molecules discovered from virtual screening and model compounds to mimic PR-104A binding. We have published two journal articles in 2012 (Acta F and PLoSONE) and have three more publications in preparation using the experimental data derived from this AMRF grant.

CAN THE ABNORMAL METABOLISM OF FIBROBLASTS FROM COPD PATIENTS BE RESTORED TO NORMAL BY REDUCING VERSICAN PRODUCTION? (1110016)

Dr Lian Wu, A/Prof Mervyn Merrilees
Dept of Pharmacology & Clinical Pharmacology, University of Auckland

Dr Lian Wu with A/Prof Merv Merrilees.

The aim of the present study was to determine whether targeting a specific protein, versican, by application of short siRNA sequences which silence genes, could reduce the abnormally increased versican production by fibroblasts from chronic obstructive pulmonary disease (COPD) patients, thereby increasing mature elastic fibre formation. As we previously reported, versican inhibits the assembly of insoluble elastin in lung. Our current results show that versican siRNA treatments effectively reduce versican mRNA expression and production, which leads to increased deposition of insoluble elastin. These findings point to a new treatment strategy for preventing or repairing elastin loss in COPD. Results from this project will be published in a peer-reviewed journal.

Grants Completed continued

NAMED FELLOWSHIPS

GOODFELLOW REPATRIATION FELLOWSHIP

TROPHOBLAST STEM CELLS IN THE FIRST TRIMESTER OF PREGNANCY (1410002)

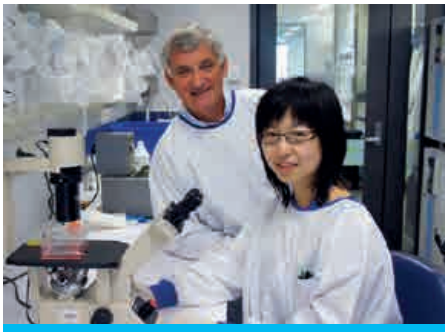
Dr Joanna James
Dept of Obstetrics & Gynaecology, University of Auckland

Dr Joanna James.

The placenta is the crucial link between the mother and baby and its growth, and development is essential for the success of pregnancy. How the placenta develops in early pregnancy is key to its ability to function successfully at the end of pregnancy, when foetal demand is greatest. However, despite our absolute reliance on it, we do not understand how the human placenta forms, or why it may fail. Trophoblasts are epithelial cells that are unique to the placenta and act to ensure a good supply of nutrients and oxygen are obtained from the maternal blood and transferred to the foetus. In this research a putative population of trophoblast stem cells was isolated from first trimester placentae. These stem cells were then compared to mature trophoblast populations to understand what makes them unique. In the future we hope to use these stem cells to study the factors that regulate the formation of different trophoblast populations in an entirely new way. This research will help us identify potential underlying causes of pregnancy disorders and may lead to new therapies for pregnancies with poor placentas.

CARRIERS FOR SKIN GRAFTS (1111012)

A/Prof Mervyn Merrilees
Dept of Anatomy with Radiology, University of Auckland



A/Prof Mervyn Merrilees with Ning Zuo in Lab.

In a previous study we developed a novel strategy for culturing skin grafts containing an increased content of elastic fibres, a key component in normal skin missing from currently available skin substitutes for grafting. Our elastin-enriched skin sheets, however, proved to be too thin for surgical manipulation and in this new project we investigated the use of two biodegradable scaffolds to act as carriers for our grafts. The first was a new wound dressing product derived from sheep foregut and produced by a NZ company, Mesynthes, and the second was electrospun mesh, made out of dissolvable suture material, and produced by Plant and Food Research at Lincoln. Both scaffolds proved to be excellent materials for the growth of our skin cells and both provided sufficient mechanical support to allow for handling and manipulations necessary for surgical use. The next phase will be testing of the grafts in wound healing models.

FUNDED BY: The William and Lois Manchester Trust.

RUTH SPENCER MEDICAL RESEARCH FELLOWSHIP

PERIOPERATIVE USE OF STATINS TO REDUCE MORBIDITY AFTER COLORECTAL SURGERY (1411001)

Dr Primal (Parry) Singh
Dept of Surgery, South Auckland Clinical School, University of Auckland

Dr Primal (Parry) Singh – Our research team at the International Surgical Week 2013 conference in Helsinki, Finland. From the left are Dr Marinus Stowers, Dr Sanket Srinivasa, myself, Professor Andrew Hill, Dr Daniel Lemanu and Dr Robert Shao.

Major colorectal surgery is associated with a high risk of developing complications which leads to significant distress for the patient and often a prolonged stay in hospital. Statins are a well-known class of cholesterol-lowering drugs that have several additional benefits such as decreasing inflammation and improving the body's response to injury and infection. Increasing evidence suggests these effects may reduce the body's stress response to surgery and thereby decrease the risk of complications. We conducted a multi-centre randomised clinical trial to investigate whether statins given around the time of colorectal surgery can reduce surgical inflammation and decrease complications. Over a two-year period we evaluated 132 patients undergoing major colorectal surgery and found that statins have a noticeable anti-inflammatory effect evidenced by a decrease in markers and clinical parameters of systemic inflammation after surgery. However, this did not translate to a reduction in complications or improvement in clinical

outcomes. Further work investigating different doses of statin treatment or evaluating their effects in other types of abdominal surgery may be useful to assess any additional benefits.

FUNDED BY: Ruth Spencer Trust

Guardian Trust

DOCTORAL SCHOLARSHIPS

INTRAVITREAL INJECTION OF CONNEXIN43 MIMETIC PEPTIDES FOR THE TREATMENT OF OPTIC NEUROPATHY USING AN IN VIVO GLAUCOMA RAT MODEL (1210003)

Miss Ying-Shan (Erica) Chen
Dept of Ophthalmology,
University of Auckland

Ms Erica Chen and her supervisor Dr Ilva Rupenthal.

Constant elevated intraocular pressure (IOP) in glaucoma causes death of retinal ganglion cells (RGC), ultimately resulting in vision loss. This study aimed to effectively deliver connexin43 mimetic peptides (Cx43 MP), which are thought to reduce RGC death and vessel leak, to the back of eye. In order to improve drug stability and tissue permeability, Cx43 MP were either chemically modified or encapsulated into polymeric particles. Particles released the drug slowly over three months and were unable to reduce the initial inflammatory response in a rat glaucoma model, only showing a delayed effect on RGC preservation. Modified peptides, on the other hand, displayed a three-fold improved half-life in ocular vitreous and spared 80% of RGC with the effect lasting for at least four weeks. A combination of these two approaches may ultimately be optimal and has the potential to save vision and reduce the treatment burden of retinal diseases by minimising the injection frequency of currently used agents.

EFFECT OF TUMOUR IDO ON HOST IMMUNOBIOLOGY (1209001)

Mr Sai-Parng (Simon) Fung
Auckland Cancer Society Research Centre,
University of Auckland

Increased levels of the enzyme indoleamine 2,3-dioxygenase (IDOl) is observed in many cancers and is strongly correlated with poor patient prognosis as this enzyme is used by cancers to suppress the immune system. This project aimed to identify novel inhibitors of IDO1 that could be developed for cancer therapy. Using differential scanning fluorimetry, we identified a number of small compounds that exhibited good inhibitory activity against the IDO1 enzyme. In silica modelling of the binding of the inhibitory compounds in the IDO1 active site allowed us to correctly predict for the functional groups and the binding orientation that causes inhibition of the enzyme. This led to the identification of a class of compounds that could strongly inhibit the IDO1 and not kill immune cells. These compounds will be used as leads to guide the rational design and synthesis of more potent, novel IDO1 inhibitors that could be developed for the treatment of cancer. Preclinical tumour models have been established to evaluate these novel inhibitors for their ability to restore tumour immunity and to augment the activity of anticancer vaccines in future work.

HUNTINGTON'S DISEASE INVESTIGATED USING A SHEEP MODEL (1209004)

Miss Renee Handley
School of Biological Sciences,
University of Auckland

Ms Renee Handley.

An effective treatment for Huntington's disease would ultimately prevent symptoms of the disease from arising. However little is known about the dysfunction that occurs in cells in the lead up to symptom onset. During my PhD I have used tissue from a sheep model of Huntington's disease to investigate molecular changes which contribute to cell dysfunction in the earliest stages of the disorder. My work has centred around two groups of sheep aged 6 months (early-life) and 5 years (mid-life). In these animals I have identified differences in the expression of several genes which are known to be affected in the end-stage human Huntington's disease brain. The results indicate that these genes may indeed be involved early on in the disease process. I have also observed changes in the abundance of a number of metabolites within brain and liver tissue from the sheep which indicate the presence of a metabolic defect. My work constitutes the first time points to be assessed as part of the ongoing characterisation of this model over its life. Critically, the protocols I have developed during my research specifically for studying sheep tissue will provide an important foundation for investigation of this model going forward.

Grants Completed continued

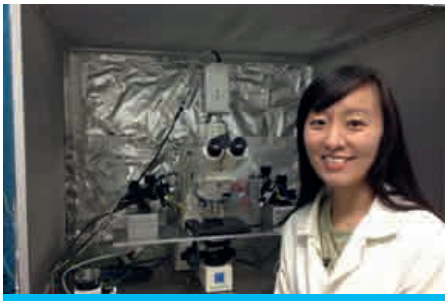
LOCALISATION OF THE CREATINE TRANSPORTER IN THE HUMAN BRAIN (1209002)

Mr Matthew Lowe
Dept of Anatomy with Radiology, University of Auckland

The aim of this project was to characterise the distribution of the proteins which control the function of creatine, an energy-supporting compound, in the brain. Creatine is currently being trialled as a therapeutic agent in Huntington's disease and Parkinson's disease. Therefore, a clearer understanding of where and how it operates is essential. The study has found that each unique brain cell in the human brain expresses a repertoire of proteins which allow the cell to use creatine specifically to meet its energy requirements. Previously, it was thought that these proteins were expressed similarly across all brain cells. This research, therefore, highlights the complexity of the brain and gives an insight into how it manages the high energy requirements it experiences.

STRUCTURAL & FUNCTIONAL DEVELOPMENT OF THE DORSAL COCHLEAR NUCLEUS IN THE MOUSE

Miss Miaomiao (Cherry) Mao
Dept of Physiology, University of Auckland



Ms Cherry Mao in Lab.

This project investigated how the first auditory nucleus in the brain which receives information from the ear develops. It focused on a small structure called the dorsal cochlear nucleus (DCN) which is an important structure in hearing but its development has been little studied. The DCN is interesting because it receives nerves not only from the ear but also from non-auditory nerves such as balance and somatosensory nerves (e.g. ones that detect body position). It is thought these non-auditory inputs are very important in shaping the physiological responses of the DCN to sound and may be important in localising where sounds are coming from. Using a mixture of techniques the study showed that, in the mouse, its gross development occurs rapidly before the ear responds to sound so that it is capable of processing sound from the environment when the ear "turns on". However, after this the responses become more complex and refined which we think is because the effect of other nerve inputs becomes more significant. This suggests that the responses of the DCN seen in the mature animal are shaped by acoustic experience rather than just sound input. These studies provide a thorough platform for further work that will investigate the effects of auditory deprivation and congenital disease on the development of the central auditory pathways.

REGULATION OF FIBRE CELL VOLUME: IMPLICATION FOR LENS TRANSPARENCY (1208003)

Miss Irene Vorontsova
Dept of Optometry & Vision Science, University of Auckland

Ms Irene Vorontsova (right) with Julie Lim and Prof Paul Donaldson.

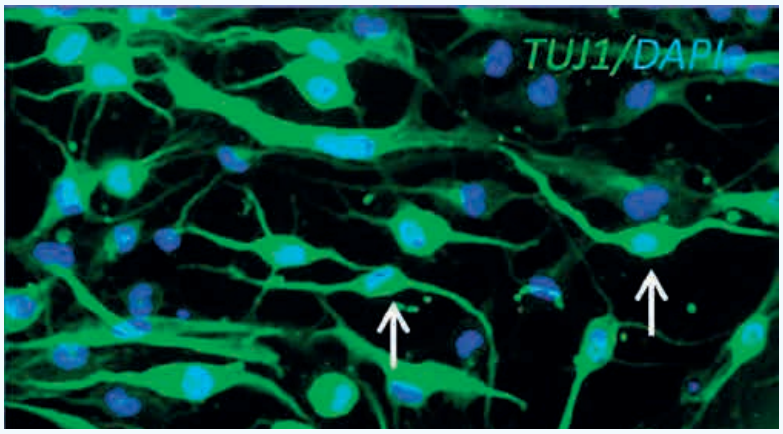
Diabetic cataract manifests as cell swelling in the lens cortex that disrupts vision. My project has extended the understanding of the molecular pathways that regulate cell volume in the lens. The two key cell volume regulatory transporters K-Cl Co-transporter (KCC) and Na-K-Cl-Co-transporter (NKCC) reveal spatially distinct activity in the lens, but act reciprocally to maintain overall lens volume. I have identified the key enzymes that regulate the activity of these transporters and shown that pharmacological manipulation of these regulators impairs the ability of the lens to regulate its volume and transparency. Future work will assess whether a dysfunction in the regulatory pathway of these transporters may be a cause for the early onset of cataract in diabetics, and whether these pathways are potential targets for development of anti-cataract therapies.

AMRF MEDICAL SCIENCES LEARNING CENTRE

University of Auckland
Faculty of Medical and Health Sciences

Opened by the Prime Minister Helen Clark in 2005, the AMRF Medical Sciences Learning Centre was funded by the AMRF to celebrate the Foundation's 50th Anniversary. The centre has won a national architecture award and houses the medical school's anatomy and pathology collections. It is used extensively by undergraduates in medicine, science and nursing from the University of Auckland and other tertiary education institutions, as well as registrars in pathology and radiology.

PUBLICATIONS



This image, from the University of Auckland's Professor Bronwen Connor, was selected for the front page of the Journal of Stem Cells and Regenerative Medicine, Volume 8, Issue 3. Her team have developed a novel technology known as direct reprogramming which allows them to generate brain cells (green) from adult human skin following over-expression of the genes SOX2 and PAX6.

Publications

Chee, K. N., **Vorontsova**, I., Lim, J. C., Kistler, J., Donaldson, P.J. (2010). Expression of the sodium potassium chloride co-transporter (NKCC1) and sodium chloride co-transporter (NCC) and their effects on rat lens transparency. *Molecular Vision,* 16:800-812.

Chen, Q., Guo, F., Hensby-Bennett, S., Stone, P., **Chamley, L.** (2012). Antiphospholipid antibodies prolong the activation of endothelial cells induced by necrotic trophoblastic debris: implications for the pathogenesis of preeclampsia. *Placenta,* 33(10):810-815.

Chen, Q., Guo, F., Liu, S., Xiao, J., Wang, C., Snowise, S., Stone, P.R., **Chamley, L.W.** (2012). Calcium channel blockers prevent endothelial cell activation in response to necrotic trophoblast debris: possible relevance to preeclampsia. *Cardiovascular Research,* 96(3):484-493.

Chen, Q., Mancy, T., Man, W., Stone, P.R., Snowise, S., **Chamley, L.W.** (2013). Calcium supplementation prevents endothelial cell activation: possible relevance to preeclampsia. *Journal of Hypertension, 31(9):1828-1836.*

Chen, Y.S., Toth, I., Danesh-Meyer, H.V., Green, C.R., Rupenthal, I.D. (2013). Cytotoxicity and vitreous stability of chemically modified Connexin43 mimetic peptides for the treatment of optic neuropathy. *Journal of Pharmaceutical Sciences,* 102(7):2322-2331.

Chung, K.K.H., **Freestone, P.S.**, Lipski, J. (2011). The expression and functional properties of TRPM2 channels in dopaminergic neurons of the Substantia Nigra of the rat. *Journal of Neurophysiology,* 106:2865-2875.

Connor, B., Maucksch, C., and Dottori, M. WO 2011/096825 A1; *Cell Programming*.

Dalbeth, N., Chen, P., White, M., Gamble, G.D., Barratt-Boyes, C., Gow, P.J., Orr-Walker, B. (2013). Impact of bariatric surgery on serum urate targets in people with morbid obesity and diabetes: a prospective longitudinal study. *Annals of the Rheumatic Diseases,* DOI:10.1136/annrheumdis-2013-203970.

Elley, C.R., Robinson, T., Moyes, S.A., Kenealy, T., Collins, J., Robinson, E., Orr-Walker, B., Drury, P.L. (2013). Derivation and Validation of a Renal Risk Score for People with Type 2 Diabetes. *Diabetes Care,* 36:3113-3120.

Flanagan, J.U., Yosaatmadja, Y., Teague, R.M., Chai, M.Z.L., Turnbull, A.P., **Squire, C.J**. (2012). Crystal Structures of Three Classes of Non-Steroidal Anti-Inflammatory Drugs in Complex with Aldo-Keto Reductase 1C3. *PLOSone,* 7(8): e43965.

Freestone, P.S, Guatteo, E., Fabiana P., di Marzo, V., Lipski, J., Mercuri, N.B. (2014). Glutamate spillover drives endocannabinoid production and inhibits GABAergic transmission in the Substantia Nigra pars compacta. *Neuropharmacology,* 79:467-475.

Fung, S-P.S., Wang, H., Tomek, P., Squire, C.J., Flanagan, J.U., Palmer, B.D., Bridewell, D.J.A., Jamie, J.F., Ching, L-M. (2013). Discovery and characterization of hydrazine as an inhibitor of indoleamine 2,3-dioxygenase (IDO 1). *Biorganic and Medicinal Chemistry,* 21(24):7595-7603.

Grant, C.C., Stewart, A.W., Scragg, R., Milne, T., Rowden, J., Ekeroma, A., Wall, C., Mitchell, E.A., Crengle, S., Trenholme, A., Crane, J., Camargo Jr, C.A. (2014). Vitamin D During Pregnancy and Infancy and Infant Serum 25-Hydroxyvitamin D Concentration. *Pediatrics,* 133(1):e143-153.

Han, C.H., Khwaounjoo, P., Kilfoyle, D.H., Hill, A., **McKeage, M.J.** (2013). Phase I drug-interaction study of effects of calcium and magnesium infusions on oxaliplatin pharmacokinetics and acute neurotoxicity in colorectal cancer patients. *BMC Cancer,* 13:495.

Jackson, V.J., Yosaatmadja, Y., Flanagan, J.U., **Squire, C.J.** (2012). Structure of AKR1C3 with 3-phenoxybenzoic acid bound. *Acta Crystallographica,* F68(4):409-413.

James, J.L., Carter, A.C., Chamley, L.W. (2012). Human placentation from nidation to 5 weeks of gestation. Part I: What do we know about formative placental development following implantation? *Placenta,* 33(5):327-34.

James, J.L., Carter, A.C., Chamley, L.W. (2012). Human placentation from nidation to 5 weeks of gestation. Part II: Tools to model the crucial first days. *Placenta,* 33:335-42.

James, J.L. (2013). Implantation. In 'Pathobiology of Human Disease: A Dynamic Encyclopedia of Disease Mechanisms'. Section Editor OM Faye-Peterson. Published by Elsevier. In Press.

Kenealy, T., **Elley, C.R.**, Collins, J., Moyes, S.A., Metcalf, P.A., Drury, P.L. (2012). Increased prevalence of albuminuria among non-European peoples with type 2 diabetes. *Nephrology Dialysis Transplantation,* 27:1840-1846.

Lorenz, N., Clow, F., **Radcliff, F.J.**, Fraser, J.D. (2013). Full functional activity of SSL7 requires binding of both complement C5 and IgA. *Immunology and Cell Biology,* 91: 469-476.

Lowe, M.T.J., Kim, E.H., Faull, R.L.M, Christie, D.L., Waldvogel, H.J. (2013). Dissociated expression of mitochondrial and cytosolic creatine kinases in the human brain: a new perspective on the role of creatine in brain energy metabolism. *Journal of Cerebral Blood Flow & Metabolism, 33:1295–1306.*

Maucksch, C., Firmin, E., Butler-Munro, C., Montgomery, J.M., Dottori, M., **Connor, B.** (2012). Non-Viral Generation of Neural Precursor-like Cells from Adult Human Fibroblasts. *Journal of Stem Cells and Regenerative Medicine*, 8(3):162-170. Front cover.

Maucksch, C., Jones, K.S., **Connor, B.** (2013). Concise Review: The Involvement of SOX2 in Direct Reprogramming of Induced Neural Stem/Precursor Cells. *Stem Cells Translational Medicine,* DOI: 10.5966/sctm.2012-0179.

McQueen, F.M., McHaffie, A., Clarke, A., Lee, A.C., Reeves, Q., Curteis, B., Dalbeth, N. (2014). MRI osteitis predicts cartilage damage at the wrist in RA: a three-year prospective 3T MRI study examining cartilage damage. *Arthritis Research & Therapy* 16:R33.

Prossler, J.E., Chen, Q., Chamley, L.W., **James, J.L.** (2014). The relationship between TGF, low oxygen and the outgrowth of extravillous trophoblasts from anchoring villi during the first trimester of pregnancy. *Cytokine, In Press.*

Reid, S.J., Patassini, S., **Handley, R.R.**, Rudiger, S.R., McLaughlan, C.J., Osmand, A., Jacobsen, J.C., Morton, A.J., Weiss, A., Waldvogel, H.J., MacDonald, M.E., Gusella, J.F., Bawden, C.S., Faull, R.L.M., Snell, R.G. (2013). Further molecular characterisation of the OVT73 transgenic sheep model of Huntington's disease identifies cortical aggregates. *Journal of Huntington's Disease,* 2(3):279–295.

Robinson, T., **Elley, C.R.**, Wells, S., Robinson, E., Kenealy, T., Pylypchuk, R., Bramley, D., Arroll, B., Crengle, S., Riddell, T., Ameratunga, S., Metcalf, P., Drury, P,L. (2012). New Zealand Diabetes Cohort Study cardiovascular risk score for people with type 2 diabetes: validation in the PREDICT COHORT. *Journal of Primary Health Care,* 4(3):181-188.

Singh, P.P., Srinivasa, S., Bambarawana, S., Lemanu, D.P., Kahokehr, A.A., Zargar-Shoshtari, K., Hill, A.G. (2012). Perioperative use of statins in elective colectomy. *Diseases of the Colon and Rectum,* 55(2):205-210.

Singh, P.P., Srinivasa, S., Lemanu, D.P., MacCormick, A.D., Hill, A.G. (2012). Statins in abdominal surgery: a systematic review. *Journal of the American College of Surgeons,* 214(3):356-366.

Singh, P.P., Srinivasa, S., Lemanu, D.P., Kahokehr, A.A., Hill, A.G. (2013). The Surgical Recovery Score correlates with the development of complications following elective colectomy. *Journal of Surgical Research,* 184(1):138-144.

Singh, P.P., Zeng, .l, Srinivasa, S., Lemanu, D.P., Connolly, A.B., Hill, A.G. (2014). Systematic review and meta-analysis of use of serum C-reactive protein levels to predict anastomotic leak after colorectal surgery. *British Journal of Surgery,* 101(4):339-346.

Singleton, R.J., Valery, P.C., Morris, P.S., **Byrnes, C.A.**, Grimwood, M.D., Redding, G., Torzillo, P.J, McCallum, G., Chikoyak, L., Mobberley, C., Holman, R.C., Chang, A.B. (2014). Indigenous children from three countries with non-cystic fibrosis chronic suppurative lung disease/bronchiectasis. *Pediatric Pulmonology,* 49(2):189-200.

Tomek, P., Palmer, B.D., Flanagan, J.U., **Fung, S-P.S.**, Bridewell, D.J.A., Jamie, J.F., Ching, L-M. (2013). Formation of an N-formylkynurenine-derived fluorophore and its use for measuring indoleamine 2,3-dioxygenase 1 activity. *Analytical and Bioanalytical Chemistry,* 405(8):2515-24.

Valery, P.C., Morris, P.S., Grimwood, M.D., Torzillo, P.J, **Byrnes, C.A.**, Masters, I.B., Bauert, P.S., McCallum, G.B., Mobberley, C., Chang, A.B. (2012). Azithromycin for Indigenous children with bronchiectasis: study protocol for a multi-centre randomized controlled trial. *BMC Pediatrics,* 12:122-131.

Valery, P.C., Morris, P.S., **Byrnes, C.A.**, Grimwood, M.D., Torzillo, P.J, Bauert, P.A., Masters, I.B., Diaz, A., McCallum, G.B., Mobberley, C., Tjung, I., Hare, K.M., Ware, R.S., Chang, A.B. (2013). Long-term azithromycin for Indigenous children with non-cystic fibrosis bronchiectasis or chronic suppurative lung disease (Bronchiectasis Intervention Study): a multi-centre, double-blind, randomised controlled trial. *The Lancet Respiratory Medicine,* 1(8):610-620.

Vialla, C.A., Chen, Q., Liu, B., Hickey, A., Snowise, S., Salmon, J.E., Stone, P.R., **Chamley, L.W.** (2013). Antiphospholipid antibodies internalised by human syncytiotrophoblast cause aberrant cell death and the release of necrotic trophoblast debris. *Journal of Autoimmunity,* 47:45-57.

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.

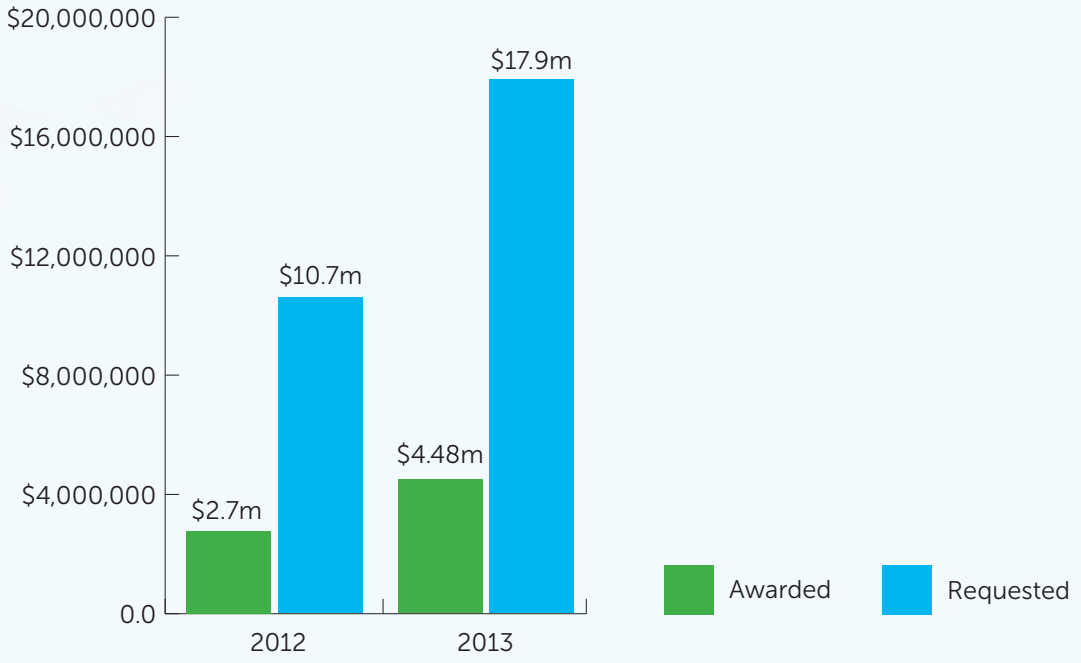
AMRF holds two free public lectures each year on topics of interest. The last lecture saw 450 general public and members gather to hear about the latest research in the area of Tinnitus.

FINANCIALS 2013

THERE ARE MANY WORTHY REQUESTS FOR FUNDING THAT WE CANNOT SUPPORT

2013 SAW A 62% INCREASE IN APPLICATIONS TO THE AMRF

2012 – $10.7 million requested, $2.7 million awarded
2013 – $17.9 million requested, $4.48 million awarded



Financial Highlights 2013

RESEARCH FUNDING 2013 $4.478M **TOTAL RESEARCH FUNDING SINCE 1955 $52.2M**

FINANCIAL PERFORMANCE

	Note	2013 $	2012 $
Income			
Donations / Subscriptions	1	173,132	129,172
Investment Income		2,147,370	2,091,623
Trust Income and External Funding	1	1,800,509	711,231
Legacies/Bequests/Specific Donations	2	444,080	1,971,552
Net Gain on realisation of investments		82,437	242,444
Net Loss on currency fluctuations		(7,250)	(7,195)
Total		4,640,278	5,138,827
Expenditure			
Operational expenses		340,278	333,591
(Less Donation)	3	(340,278) Nil.	(333,591) Nil.
Research Grants 2013	4	4,263,479	2,721,784
Depreciation on Grant Funded Assets		4,857	6,253
Reduction in value of investments		461,791	118,595
Total		**4,730,127**	**2,846,632**
Net (Deficit) / Surplus		**(89,849)**	**2,292,195**

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: 09 923 1701 or Email: amrf@medicalresearch.org.nz

	2013	2012
Donations / Subscriptions	$173,132	$129,172
Investment Income	$2,147,370	$2,019,623
Trust Income and External Funding	$1,800,509	$711,231
Legacies / Bequests / Specific Donations	$444,080	$1,971,552
Net Gain on realisation of investments	$82,437	$242,444

NOTES TO THE 2013 FINANCIAL REPORT

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

Guardian Trust Administered Funds	
David & Cassie Anderson Medical Trust	186,640
Angus Family Trust	103,000
Barbara Basham Medical Trust	126,000
Jean Cathie Research Trust	165,484
Henry Cotton Charitable Trust	126,000
The Clyde Graham Charitable Trust	8,000
Edith C Coan Trust	120,000
TM Hosking Charitable Trust	20,000
John A Jarrett Trust	40,000
Rose Richardson Estate	34,000
The Richardson Trust	4,983
The J&P Stilson Endowment Trust	138,893
The Ruth Spencer Estate	257,333

Public Trust Administered Funds	
Acorn Charitable Trust	10,000
Ralph Dingle Trust	2,000
The Reed Charitable Trust	4,000
Audrey Simpson Trust	3,545
Tennyson Charitable Trust	5,000
Wellington Sisters Charitable Trust	5,000

Other Trusts/Funds	
Anonymous	376,437
The William and Lois Manchester Trust	40,964
The Marion Ross Memorial Fund	75,230
Rotary Club of Auckland Harbourside	40,000
Paul Stevenson Memorial Trust	30,000

2. Legacies, Bequests and Specified Donations 444,080

Estate of Peggy Butler	Estate of Marie Mabel
Estate of Maureen Cannon	Estate of Robert MacGillivray
Estate of Margaret Carless	Estate of V C Purkis
Estate of Zena Elsie	Estate of Elaine M Robinson
Estate of Goodey	Estate of Patricia Snowden
Estate of Thelma Judd	Estate of Christina Wishart

3. Operational Expenses

The Foundation is very grateful for the Harry Goodfellow Fund, Hector Goodfellow Fund and TB & WD Goodfellow Funds for the external funding of operational expenses in 2013.

4. Research Funding Approved During Year

RESEARCH PROJECT GRANTS (28)	
AMRF General Purpose & Named Funds Supporting Research Projects	2,552,107
A C Horton Estate	
Breast Cancer Research Fund	
Brian Jones Fund	
Doug Brown Fund	
GS Blanshard Fund	
Hugh Green Diabetes & Breast Cancer Fund	
LH Corkery Fund	
MJ Merrilees Fund	
Sir Henry Cooper Fund	
Sir Lewis Ross Fund	
Sir William Goodfellow Fund	
W & WAR Fraser Fund	
Other Trusts & Estate Income Supporting Research Projects	
Angus Family Trust	103,000
Jean Cathie Research Fund	166,484
REPATRIATION FELLOWSHIP (1)	
Goodfellow Repatriation Fellowship	376,437
MEDICAL RESEARCH FELLOWSHIP (1)	
Ruth Spencer Medical Research Fellowship	257,333
POSTDOCTORAL FELLOWSHIPS (2)	
David and Cassie Anderson Research Fellowship	186,640
Edith C Coan Research Fellowship	196,000
DOCTORAL SCHOLARSHIPS (4)	
AMRF Doctoral Scholarships (2)	252,000
Barbara Basham Doctoral Scholarship	126,000
Henry Cotton Doctoral Scholarship	126,000
AMRF TRAVEL GRANTS (39)	97,959
OTHER GRANTS (3)	
Gavin and Ann Kellaway Medical Research Fellowship (1)	12,943
HealtheX Emerging Research Award (1)	5,000
Sir Harcourt Caughey Fund (1)	20,294
Total Grants Committed 2013	4,478,197
Less amounts allocated but not required	(214,718)
TOTAL GRANT FUNDING 2013	**4,263,479**

Members & Supporters 2013

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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Estate of Margaret Carless
Estate of Veronica Catherine Purkis
Estate of Goodey
Estate of Marie Mabel Hall
Estate of Thelma Judd
Estate of Robert L MacGillivray
Estate of Elaine M Robinson
Estate of Zena Elsie Robinson
Estate of Patricia Snowden
Estate of Christina Wishart

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A recent quote from Elspeth Mount QSM, about becoming an AMRF member:

"I am absolutely in awe of the work of AMRF to date and would certainly encourage every member to help spread the word and seek to grow the membership among their family, friends and colleagues".

When you become an Annual or Life Member of the Foundation you will receive access to the latest information in the research world, hard copies of the AMRF's biannual Newsletter and Annual Report, and access to lectures and member only events. Sign up online or complete the form below.

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You may consider a Remembrance Donation in lieu of flowers or may wish to honour a special occasion such as the birthday of a friend or family member. The Foundation will send a personalised letter advising that you have made this type of donation. Such donations are appreciated by the individuals or families as this is a dignified and practical way of expressing your condolences or celebrating a special occasion.

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A bequest is a gift of cash or assets (shares, property, or other assets) made through your Will. A bequest or major gift to the AMRF is an investment in the health of future generations. You can choose to leave your gift for a specific area of research or for general purposes, allowing the Foundation to determine the greatest area of need. If you are considering this option please contact us, as we are happy to assist.

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