Eyeing up Regenerative Medicine

Regenerative medicine aims to replace cells and tissues lost during disease progression, ultimately aiming to restore function back to pre-disease levels. Stem cell research is one of the main focal areas offering hope in the field of regenerative medicine and one area already using adult stem cells for repair is in the eye.

The cornea is the front transparent surface of the eye. Its transparency is crucial for light entering the eye and for the focusing of light onto the photoreceptors in the retina. Specialised adult stem cells that are abundant at the limbus have important functions within the retention of normal corneal integrity and repair upon injury. Limbal Stem Cell Deficiency (LSCD) leads to vision impairing disabilities which severely affect the patient’s independence and quality of life. Treatment for LSCD patients has long been frustrating with many patients having a poor prognosis.

Recent advances in therapeutic options for LSCD patients use an autologous graft of the patients’ own limbal stem cells following expansion in the laboratory. However this form of autologous transplant is highly undefined and has varying levels of success.

A new study, funded by the AMRF, proposes a new unit of tissue for transplantation that will provide a highly defined transplantable entity for implantation at a defined site (the limbus) that may have the potential to restore the limbus to near-pre-LSCD condition. Achievement of this will not only correct the current defect for the patients but may also provide the eye with restored long term ability to heal itself.

AMRF Artworks Charity Dinner

AMRF is pleased to have been selected as the beneficiary of the 2011 Artworks Charity Dinner, and would like to thank the Friedlander Foundation for their support. Artworks is a Rotary initiative that aims to celebrate the vision and creativity of New Zealand artists and take New Zealand and Pacific art to the world. It has taken place annually from 2002-2008 and has provided artists with over $1.7 million of income, and raised over $1.1 million for charitable causes. As well as online, it will be staged at St Matthew in the City this year and will feature a week of exhibitions and festivities.

Thank you to all those who have purchased tables and donated auction items. Funds raised will be tagged for research into Stem Cells & Regenerative Medicine.

Proudly supported by the Friedlander Foundation.

Your donation to AMRF goes directly to fund research – not administration

The Auckland Medical Research Foundation (AMRF) is the longest running independent funder of medical research in the greater Auckland region. Established in 1955, we distribute over $3 million annually to a wide range of research projects. A generous endowment to the AMRF funds all of our administrative overheads and running costs. This means that 100% of every donation made by individuals, companies and organisations goes directly to support research and not administration.
Dr Wayne Patrick with his PhD students Paulina Hanson-Manful and Valerie Soo.

After eight years overseas as a PhD student and post-doctoral fellow, Dr Wayne Patrick arrived home in New Zealand in late 2007. He had accepted a position as lecturer in Biochemistry at Massey University’s Albany Campus, and he had grand plans for launching an independent research career at the intersection of biomedical science and evolutionary biology. One particular focus was to explore the evolution of antibiotic resistance in bacteria. Today, many antibiotics have lost their power. Disease-causing “superbugs” evolve resistance faster than we can develop new drugs.

Where does all this antibiotic resistance come from? In 2008, Dr Patrick received a project grant from the Auckland Medical Research Foundation to measure the latent potential of a model bacterium (Escherichia coli) to evolve resistance. The grant enabled him and his first two PhD students, Valerie Soo and Paulina Hanson-Manful, to test every gene in the E. coli genome for its ability to confer resistance, under each of 237 different antibiotic treatment regimes. Experiments on this scale had never been attempted before.

In his AMRF grant proposal, Dr Patrick confidently predicted that he would “uncover many examples” of novel resistance genes. What he certainly did not expect was to find over 100 of them! By amplifying and speeding up the process of microbial evolution, Soo, Hanson-Manful and Patrick discovered a range of genes that had never previously been associated with drug resistance. Many of the changes in resistance that they observed were too small to be relevant in the clinic. Nevertheless, Dr Patrick and his team had mimicked plausible first steps towards full-blown resistance, and shown that the genomes of bacteria code for an enormous reservoir of latent resistance genes. In January of this year, the research findings were published in the prestigious science journal, Proceedings of the National Academy of Sciences USA.

The implication is that the bacterial drug resistance problem is going to worsen. Ultimately, Dr Patrick hopes that his study will galvanize pharmaceutical companies (many of whom are closing their antibiotic discovery pipelines) back into action. He also expects that his team’s high-throughput approach will prove useful for predicting whether resistance is likely to evolve towards new drugs that are being developed. In turn, this will give an indication of whether new antibiotics will be effective in the clinic for short or – hopefully – long periods.

Dr Shirley Tonkin with AMRF Researchers Dr Christine McIntosh and Prof Alistair Gunn.

Paediatrician Dr Shirley Tonkin visited the AMRF offices earlier this year.

Dr Tonkin is an independent research consultant and has been a co-applicant on medical research funded by the Auckland Medical Research Foundation working with Professor Alistair Gunn researching the benefits of car seat inserts, and with Dr Christine McIntosh researching whether pacifiers can reduce the risk of upper airway obstruction in infants.

To avoid this problem Dr Tonkin’s team developed an insert for car seats which supports the baby’s body forward, so that the head can stay in its natural position when the baby is strapped in. The pacifiers and infants airway study is ongoing with the aim of seeking to identify the mechanism whereby sucking on a pacifier decreases the risk of Sudden Infant Death Syndrome (SIDS).

Jeff Todd Recently Appointed President of AMRF

Throughout the 56 year history of the Auckland Medical Research Foundation, our research efforts have been targeted at improving the health and well-being of all New Zealanders. From the beginning, the research work of the Foundation has been supported and directed by the AMRF Board of Trustees drawn from the professional, business and medical communities of Auckland.

As recently-appointed President of the AMRF, I look forward to serving the best interests of the AMRF with my fellow Trustees and our dedicated Medical Committee who play a crucial role in attracting and evaluating applications for research funding and support. Having served on the Board since 2003, I bring to the President’s role experience of the Foundation’s operations and achievements and an understanding of the great opportunities before us. I also bring recent experience in governance with other business, medical research and charitable organisations.

The outstanding contribution to the Foundation made by the late Mr Bruce Cole and his predecessors as Trustees over the years provides a firm base on which the AMRF will build for the future. I look forward to contributing to that bright future and the continuing success of the Foundation.
A/Prof Carolyn (Raina) Elley, Mrs Elizabeth Robinson,

**DIABETES CVD RISK EQUATION VALIDATION**

We have identified a new protein, called PGAF, that plays a critical role in maintaining the integrity of the kidney's blood filters. By understanding how PGAF functions we hope to develop new therapies to preserve kidney function in patients with chronic kidney disease.

**VACCINATION AGAINST GAS**

Dr Fiona Radcliffe, A/Prof Thomas Proffit, Prof John Fraser

Dept of Molecular Medicine & Pathology, The University of Auckland

Streptococcus pyogenes, or group A streptococcus (GAS), is an important human pathogen responsible for a wide range of diseases from minor throat infections to life threatening flesh-eating disease. There is no vaccine available for GAS and several promising candidates have failed to reach the clinic because of cross-reactivity with human tissue. We have identified a virulence factor, SpnA, which is expressed in all clinical isolates and is associated with pathogen survival in human blood. Patients do develop specific immune responses (antibodies) which can inhibit the activity of SpnA, but this response is generally transient and present immediately after infection. We aim to test whether we can elicit a robust and durable antibody response to SpnA by combining it with an in-house vaccine carrier, M1. The M1 carrier targets immune cells called antigen-presenting cells, leading to improved delivery of vaccine candidates and vaccine carrier, M1. The M1 carrier targets immune cells called antigen-presenting cells, leading to improved delivery of vaccine candidates and enhanced immune responses. Vaccine preparations will be tested in mice and if this approach shows potential, the mice will be infected with GAS to determine whether vaccination to SpnA stimulates protective immunity. These studies will enable us to test the potential of a novel vaccine candidate for GAS, a significant human pathogen.

**PGAF AND RENAL DISEASE**

A/Prof Alan Davidson

Dept of Molecular Medicine & Pathology, The University of Auckland

New Zealand has alarmingly high rates of chronic kidney disease, particularly amongst the Maori and Pacific People where diseases such as diabetes and hypertension damage the blood filters in the kidney. We have identified a new protein, called PGAF that plays a critical role in maintaining the integrity of the kidney's blood filters. By understanding how PGAF functions we hope to develop new therapies to preserve kidney function in patients with chronic kidney disease.

**Diabetes CVD Risk Equation Validation**

A/Prof Carolyn (Raina) Elley, Mrs Elizabeth Robinson, A/Prof Tim Kenealy, Dr Sue Wells, Dr Paul Drury, Prof Bruce Arroll

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

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 published a new risk equation, using recent New Zealand data. The new equation suggests that we are currently under-treating certain groups in New Zealand (NZ), including people with poorly controlled diabetes or kidney impairment, especially for Maori, Pacific and Indian populations. This proposal aims to validate the new risk equation using clinical data from general practices in NZ to ensure it is more accurate than the US equation. We also propose to develop and test a new open-access web-based risk calculator based on the new NZ risk equation.

**Induced Neural Precursor Cells**

Dr Bronwen Connor, Dr Christof Maucksch, Dr Mirella Dottori, A/Prof Chris Print

Dept of Pharmacology, The University of Auckland

It has long been considered that once a cell reaches maturity it is unable to change to a different cell type. However, 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 forced expression of specific genes (reprogramming). Advancing this capability, we propose it is possible to convert one cell type to another directly, without the need to first revert the cell to a pluripotent stem cell state.

Ruth Spencer Medical Research Fellowship

Dr Primal Singh

Dept of Surgery, South Auckland Clinical School, The University of Auckland

With New Zealand having one of the highest incidence rates of colorectal cancer in the developed world, colorectal surgery is among the most common major operations performed in the country. Although surgery can provide a cure for colorectal cancer, it has a high risk of developing serious complications which leads to significant distress for the patient and often a prolonged stay in hospital. The body’s response to surgery, which involves inflammation and hormonal changes, increases the risk of developing such complications and reducing this ‘stress response’ is shown to be beneficial. Statins are a widely used class of cholesterol-lowering medication that have 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 therefore decrease the risk of complications developing after surgery. We aim to explore these benefits of statins by conducting a study that investigates their use in patients undergoing colorectal surgery. If statin use can decrease the morbidity associated with colorectal surgery, it would significantly improve patient care and lead to better health outcomes.

**JUNE 2011 GRANT ROUND AWARDS OVER $1.13 MILLION**

The AMPF’s June grant round again saw a record number of grants received by the Medical Committee for consideration where more than $1.13 million in funding was distributed over a wide range of medical research. Awards included 10 full project grants, a Ruth Spencer Fellowship and 10 Travel Grants.

A selection of project grants and the Ruth Spencer Fellowship are summarised below:

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A/Prof Alan Davidson

Dept of Molecular Medicine & Pathology, The University of Auckland

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**Funded by Hugh Green Diabetes & Breast Cancer Research Fund**

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This project aims to establish an innovative approach for generating immature brain cells (neural precursor cells) directly from adult human skin. Of major significance is that this will avoid the need to generate an intermediate embryonic stem cell phase, providing neural precursor cells for research and therapeutic applications without risk of tumour formation from pluripotent stem cell contamination. This project will establish cell reprogramming as a key capability in New Zealand. The ability to directly generate human neural precursor cells offers a powerful system for studying brain development, modeling neurological disease, drug discovery and eventually, cell replacement therapy.

**RUTH SPENCER MEDICAL RESEARCH FELLOWSHIP**

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FREE PUBLIC LECTURE

Eyeing Up Regenerative Medicine

By Associate Professor Trevor Sherwin

Associate Professor Trevor Sherwin will outline the emerging area of regenerative medicine with a focus on eyes. Trevor will illustrate his presentation using recent data involving human stem cell transplantation to restore vision in patients with stem cell deficiency in the eye.

WHERE: Lecture Room OGGB4
The University of Auckland Business School
Owen G Glenn Building
Grafton Road, Auckland

WHEN: Thursday 27 October 2011, 6:30pm

ENQUIRIES: Kathleen 09 923 1701
or visit our website www.medicalresearch.co.nz

Q & A:
TIME SET ASIDE FOR QUESTIONS FROM THE AUDIENCE

Parking is available under the Owen G Glenn Building. It is assessed from Grafton Road at the traffic lights opposite the on-ramp to the Port. Cost is $5 after 5pm for the evening. Payment for parking is by cash, Visa, or MasterCard only.

Young AMRF Researchers Gain Top Honours For Research

Dr Benjamin Thompson (Dept of Optometry & Visual Science, University of Auckland) received an Early Career Research Excellence Award, May 2011, for his work on the treatment of amblyopia (or lazy eye) in adults and the effects of a novel "at home" treatment using an iPod touch device.

Dr Isuru Jayasinghe gained one of the five Vice Chancellor’s Prizes for Best Doctoral Thesis (2010). This prestigious award was given to Dr Jayasinghe who wrote his thesis on Resolving the Structural Basis of Cardiac Excitation-contraction Coupling.

Obituary

Bruce Sterling Cole
1 July 1926 – 11 May 2011

Bruce Cole, our respected President and long serving Trustee of the Auckland Medical Research Foundation (AMRF) - March 1991 to May 2011.

Bruce joined the AMRF Board in March 1991 and was President from May 2002 until his death on 11 May 2011. Bruce had an outstanding business career and his business acumen coupled with his passion for research underpinned AMRF’s success in becoming the leading independent organisation funding medical research in the greater Auckland region. Bruce’s leadership, drive and guidance enabled the AMRF to provide a secure environment and tenure for emerging medical researchers which is so important in retaining the country’s best and brightest scientists in New Zealand. Bruce was also personally responsible for the Foundation’s support in 2005 for the establishment of the AMRF Medical Sciences Learning Centre alongside the Faculty of Medical and Health Sciences. This Centre has provided an inspirational learning environment for medical students.

The Trustees, Medical Committee and staff of the AMRF pay tribute to Bruce. The Foundation received enormous benefit from his quiet and unassuming leadership spanning some twenty years.

Bruce is survived by his wife Noel, Nicholas and Sarah, Alex and James and their families.

Auckland Medical Research Foundation

Yes! I would like to support the Auckland Medical Research Foundation.

As a donor:    $1000    $500    $100    $50    $ ______ is the donation of my choice

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Expiry ______ / ______ Signature ____________________________

Initials & Name: ____________________________    Phone: ( ) ____________________________

Address: ____________________________    E-mail: ____________________________

• Every dollar donated goes to medical research

• Donations of $5 or more are receipted and tax deductible