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Chairman's Report 2009

This year has seen a reduction in the amount of research the Foundation has been able to fund which is disappointing but very prudent fund management by the Finance and Investment Committee (headed by Warwick Aitken) has seen our portfolio gain in value by 4.3%. This is of course on a background financial climate where most investors faced significant negative returns.

Once again we are most grateful for substantial support from Trust Waikato and also the Waikato / Bay of Plenty Division of the Cancer Society and Braemar Charitable Trust. As indicated in the last annual report we are making steady progress towards marketing and fundraising with the completion of a database of previous donors and potential new donors with the assistance of Gordon Chesterman and Selina Corboy.

It is vital for the maintenance of high levels of patient care in Waikato that our Foundation enlarge its portfolio.

Availability of research funds locally helps attract and retain high quality scientific and medical staff. Being able to support PhD students has been very rewarding. Dr Rathan Subramaniam who completed his PhD lat year achieved one of five "best thesis" awards for his work from Auckland University. It is remarkable how well Dr Martyn Harvey has progressed towards his PhD with his work supported by the small grants he has been awarded from our Fund.

On the other hand, it is once again disappointing how little HRC funding comes to the Waikato. This underscores the need for a much stronger Waikato Medical Research Foundation.

There has been no change in the Trustees this year. Their time is freely given but most valuable. Once again, our Patron Peter Rothwell's contribution is highly valued.

The Grants Committee has the unenviable task of sorting grants according to scientific merit and allotting meager funds. This means that we cannot support all worthy applications and only the top proposals receive money. I thank Adrian Molenaar and his committee for their time and expertise.

The only change to account is a change in administrator from Fiona Williams, who moved much further south, to Robyn Fenneman. We welcome her to her post.

The most important part of the report is of course to thank all donors, big and small. Without your support local research would suffer greatly.

Dr Noel Karalus
Chairman

Year 2009 **Report of the Grants Committee**

This year we received 9 applications requesting a total of $201,335. With additional support as detailed in the Chairman's report, the WMRF was able to offer just over $115,000 among 8 applications. Most of the applications were cross institutional in the Waikato research community.

This year the successful applications included projects on; colorectal cancer, wound healing, inflammatory bowel disease, anesthesia related heart attacks, brain seizures, mental illness, and treatments for low blood sugar in babies.

With the seed support from the WMRF, many of these projects generate data for more substantial support elsewhere and are translated into useful tool products and services relevant to the Waikato community and beyond.

I thank; Maggie Fisher, Amanda Oakley, Roy Daniels, Richard Bedford and Michael Jameson from the Grants Committee, and Warwick Aitken from the Finance Committee who helped assess the applications this year, the Foundation chair, Noel Karalus for his input and approaches to other funding bodies, and Robyn Fenneman for her administrative support.

Adrian Molenaar

Chair, Grants Committee

Reports from 2008 Grant Recipients

Reports from 2008 Grant Recipients

Disarming Pathogens with Natural Products from Milk

Investigators: *Paul Harris, AgResearch Ltd, Ruakura*
Jenna Signal, University of Waikato

Background

Antibiotics that are available today are primarily targeted at bacterial viability. Although this mode of action is highly effective, it also imposes selective pressure that fosters the growth of antibiotic-resistant strains. There is, however, an alternative approach which is geared at 'disarming' pathogens by inhibiting virulence factors. This is one way in which host defence mechanisms keep pathogens at bay. Milk contains a number of antimicrobial substances, some of which may act by disarming pathogens.

Objective

Our objective was to establish in our lab an in vivo nematode model of persistent infection, and to use this model to test selected milk-derived proteins for anti-virulence properties.

Results

We found that several, but not all, of our selected proteins gave a protective effect against a persistent infection by *Enterococcus faecalis*. One milk protein in particular was active at very low concentrations and prevented bacterial colonisation throughout the time course of the study, in a similar manner to the antibiotic control. Other milk proteins were active only at higher concentrations, and in some cases lost their protective effect after a time point. A time course study revealed different colonisation patterns when infected nematodes were treated with different milk proteins. In some cases, the test proteins prevented and maintained low levels of colonization throughout the entire time course. Other proteins, however, were unable to prevent an initial colonisation but could later reduce the level of colonisation with time.

During the initial development of the model we serendipitously discovered that some milk proteins also gave a protective effect against an unknown Gram negative bacterial contamination. Also, some proteins were effective against *Enterococcus* but not the Gram negative organism. This will be followed up in future work.

We also discovered that one milk protein gave an unusual and unexplained morphological change in the nematode. The significance of this is not known at this stage.

Conclusions

This work has established a working in *vivo* model of persistent infection in our lab. This has been used to identify several milk-derived proteins with potential anti-virulent activities. Furthermore it has revealed interesting time course colonization patterns with different proteins treatments. We intend to follow-up these initial studies using this model in on-going work in our lab.

Reports from 2008 Grant Recipients

Waikato Medical Research Foundation Grant #153 (2008)
Interim Report
Lead Investigator: Gerard P. Devlin, MB ChB BAO FRACP

Background

This grant provides partial funding for a study to investigate the role of myostatin in the ischaemic heart. Myostatin is a key regulator of muscle development which inhibits the development of skeletal muscle principally by blocking the recruitment and proliferation of specialised stem cells.

A previous study by this group showed that expression of myostatin is increased in the peri-infarct region of the heart after myocardial infarction (MI), which supports the notion that myostatin plays a central role in regulating cardiac muscle in the ischaemic penumbra. This study investigates the hypothesis that myostatin acts to block stem cells from being recruited into the infarcted area after MI, thereby preventing growth of replacement muscle tissue.

Should this hypothesis be proven, development of a myostatin inhibitor for post-infarct administration would result in fewer people who suffer a heart attack going on to suffer the poor quality of life and disability associated with heart failure, and would greatly reduce spending on hospital admissions due to heart failure, releasing health funding for other purposes.

Progress

A requirement was imposed by the Ruakura Animal Ethics Committee that the group first carry out a pilot study on a small number of mice, and that a report be submitted to the Committee prior to authority for the main study being granted. The pilot study also provided the opportunity to develop the required surgical and ultrasound techniques on mice.

Open-chest surgery on mice proved to be a difficult technique to perfect, and considerable time was expended in refining the procedures, including a visit to Christchurch School of Medicine to observe similar procedures being carried out there. Also during the pilot study, it was found that the group's cardiac ultrasound machine was not capable of being updated to operate at a frequency sufficiently high to image the rodent heart, which beats in the order of 400 beats per minute. This led to a significant delay in proceeding with the pilot study, since further funding for a replacement ultrasound machine had to be sought. Dr Devlin successfully obtained partial funding from the Heart Foundation and Dr Lim obtained a grant for the balance from the Royal Australasian College of Physician (RACP) General Endowment Fund. A used Philips HDI500 ultrasound machine was purchased from Philips Medical Systems, who also provided training for Dr Lim in its use. The machine provides excellent imaging of the mouse heart.

The time spent awaiting grant application results was not wasted. RNA was extracted from ovine cardiac tissue obtained during a previous study at various time-points (control, 6 hours, 12 hours, 1 day, 2 days, 4 days and 8 days) post-infarct, both peri-infarct and distal to the infarct, and the concentration of myostatin over time post-infarct in these areas was quantified using real-time PCR techniques. Results are presented below.

Once the ultrasound machine was available and Dr Lim was fully trained in its use, the pilot study continued until all requisite techniques were operating routinely. At this point, a report was submitted to the Ethics Committee and authority to commence the main trial was granted.

The main study is now under way, and some preliminary data are available, which are presented in the Results section below. The delays reported above mean that the study will now not be completed until probably this time next year.

Reports from 2008 Grant Recipients

Are gap junctions important in neocortical seizures? (WMRF Grant 139)

Dr Jamie Sleigh

Section 3 – Research Progress

Dr Jonathan Mason arrived from the USA in June 2008 and was employed in the Dept Engineering at the University of Waikato for a year. He has recently returned to the USA. Half his salary was for teaching relief (funded from a Marsden Grant), and the other half from the Waikato Medical Research Foundation for research time. We have managed to establish a breeding colony of gap junction (connexin-36) knockout mice at the Ruakura secure facilities and have made good progress with measuring the effects (and lack of effects) of various gap junction modulators. We have found that neocortical slices from gap junction knockout mice have smaller seizure-like events and are resistant to the pro-seizure effect of the anaesthetic drug etomidate. These pro-seizure effects are mediated via GABAA receptors, and do not seem to be influenced by alterations in chloride or calcium homeostasis.

Initially Dr Mason encountered some difficulty in the software implementation of the protocol required to control the somewhat delicate (but very accurate) electrical stimulation and recording hardware (Agilent E5270B). However these difficulties were eventually overcome and he has obtained reliable recordings from a number of neocortical slices. This electrical impulse data requires further analysis and development of new stimulus protocols; and we hope that this will form the basis of a future PhD thesis by Mr Maher Elbohouty.

Research Outputs

Research Publications: Two papers are in preparation and should be submitted for publication in the next few months.

Dissemination & Implementation of Research Results: We plan to present these results at neuroscience conferences later this year, and next year at the AWBRC.

Reports from 2008 Grant Recipients

The evaluation of the BK channel as a possible drug target for the treatment of tremor, ataxia and heart conditions

Dr Sarah Finch - AgResearch, Hamilton.

Ion channels are the fundamental elements that underlie signalling in nerve and muscle cells. They are protein molecules that form hydrophilic pores that can open and close to allow ions to flow across cell membranes. BK channels (large-conductance calcium-activated potassium channels) are present in many tissues and regulate important physiological processes.

Due to the importance of BK channels extensive research has been conducted to determine its structure and function using compounds which affect channel opening and closing. We have recently discovered that the toxin responsible for ryegrass staggers in New Zealand (lolitrem B) is the most potent non-peptide inhibitor of the BK channel yet discovered and that the tremors and ataxia induced by this toxin are mediated specifically through the BK channel. We have also found that BK channel blockers have a direct effect on the heart to decrease heart rate. This was very surprising since it has long been accepted in the ion channel field that BK channels are not present in the heart.

These observations show the BK channel to be a potential drug target for the treatment of disorders involving tremor, ataxia and heart rate. To test the feasibility of this approach, BK channel modifying agents were used to determine whether the tremor, ataxia and heart rate effects induced in mice by lolitrem B and the related compound, paxilline could be altered. This was achieved by using an accelerating rotarod to measure ataxia, and a non-invasive blood pressure/heart rate analysis system to measure heart rate.

Dosing mice with NS1619, a BK channel opener, prior to a paxilline challenge showed that the severity of tremors induced by paxilline could be reduced. It was very interesting to note, however, that the heart rate decrease induced by paxilline was unaffected by pre-dosing NS1619 at the dose rates given.

Aminooxyacetic acid (AOAA) was also pre-dosed to mice. AOAA increases brain GABA levels and we thought that this may compensate for the cerebellar disinhibition caused by the BK channel blocker, paxilline. Results showed that pre-dosing with AOAA caused a significant decrease in the tremor induced by paxilline. However, no significant effect of AOAA on either the motor function deficits or the heart rate effects induced by paxilline were observed.

This project has yielded important and interesting results. Tremors induced by the BK channel blocker, paxilline, could be altered by both the BK channel opener, NS1619 and the GABA modulator, AOAA whereas no effect was observed on the ataxia or heart rate effects. This suggests that the tremor, ataxia and heart rate effects are induced by different mechanisms on the BK channel. Further work is planned looking at additional BK channel activators with differing specificities and additional drugs to alter brain GABA levels.

Reports from 2008 Grant Recipients

Interim Report: Prophylactic Antibiotics in Simple Trauma WMRF #146

Dr Martyn Harvey

Traumatic wounds requiring surgical closure represent a common Emergency Department presentation. Development of secondary infection may significantly prolong wound healing and contribute to additional morbidity. The utilization of prophylactic antibiotics in simple traumatic wounds is however controversial, with no data clearly endorsing antibiotic administration. Studies to date however have largely examined antibiotic administration at the time of wound closure.

We postulated potential reduction in wound infection with antibiotic administration at the earliest possible juncture following injury. Practically, this is represented by the time of initial presentation to the Emergency Department. The current study of prophylactic antibiotic administration at initial Emergency Department triage is underway with the goal of further exploring this hypothesis. If proven, early administration of antibiotic treatment may reduce complications related to wound infection.

The present study is a randomised, controlled, double blinded, clinical investigation of antibiotic administration at triage in simple traumatic wounds. Enrolment via the Emergency Department of Waikato Hospital, and data collection, is current and ongoing. It is anticipated that a final report be lodged in the 2010 Waikato Medical Research Foundation Annual Report.

Successful triage of patients referred to a skin lesion clinic using teledermoscopy (IMAGE IT trial).

*E. Tan, A. Oakley, M. Rademaker, A. Yung and M. Jameson**

Departments of Dermatology and Oncology, Waikato Hospital, Hamilton, New Zealand*

Teledermoscopy was assessed as a triage tool for patients referred to a hospital skin lesion clinic. Digital photographs were taken of skin lesions of concern and the patients were then seen face-to-face by two dermatologists independently. The digital images were evaluated 4 weeks later, as a teledermoscopy consultation, by two experienced dermatologists. The diagnosis and management of skin lesions from both types of consultation were compared.

Two hundred patients with a total of 492 lesions were seen. The mean age of participants was 60 years. There were a total of 116 skin cancers (14 melanomas, 62 BCC, 15 SCC, 25 Bowen's) and 119 premalignant lesions (13 atypical naevi, 106 actinic keratoses) diagnosed on the face-to-face consultation. The rest of the lesions were benign (240 lesions: 109 melanocytic naevi, 101 seborrhoeic keratosis and 30 other lesions).

There was excellent agreement between teledermoscopy and face-to-face diagnosis for all lesions, with only 9% of lesions having disparate diagnoses of clinical significance. Eight of 492 lesions were underreported by teledermoscopy when compared to face-to-face diagnosis but when histopathology became available, only 1 malignant lesion had been missed (a BCC diagnosed as solar keratosis) by teledermoscopy.

Teledermoscopy approximated 100% sensitivity and 90% specificity for detecting non-melanoma and melanoma skin cancers. Importantly, 74% of all lesions were determined by teledermoscopy to be manageable by the General Practitioner without needing to be seen face-to-face by a dermatologist. This use of teledermoscopy as a triage tool offers the potential to shorten waiting lists and thus improve healthcare access and delivery.

Abstracts of 2009 Grant Recipients

Abstracts of 2009 Grant Recipients

Comparison of dairy and soy protein in a model of gastrointestinal inflammation

Alison Hodgkinson

Abstract

The food we eat has a great influence on our health and well being. Equally, our health status has an impact on how we process that food. We need our digestion system to be in good shape so that what we eat is processed efficiently and effectively. Like the rest of our body, the health of our digestive tract is maintained by our body's immune system. However, a fine balance is required to maintain a healthy gut environment. Most foods we eat are harmless and though recognised as foreign to the body, the immune system does not react to them. On the other hand, the body must be able to recognise bacteria and toxins that may be present in contaminated food and react appropriately to eliminate the danger. This balance is maintained by a complex interaction between specialised cells of the immune system and chemical messengers, called cytokines. If the balance is disrupted this may cause inappropriate reactions to food and lead to diseases like Inflammatory Bowel Disease (IBD).

One cytokine plays a pivotal role in dampening down and suppressing inflammatory reactions in the body. Specially bred mice that are unable to make this cytokine, spontaneous develop IBD. This mouse breed has been used by researchers to study the inflammatory processes involved in IBD development.

In our research, we are investigating aspects of milk allergy in the gut. We looked at the effects of milk in the gut using the specially bred mice, comparing mice fed a diet containing milk protein or soy protein. The milk-fed mice did not thrive well, which was not surprising in these disease-prone mice. On the other hand, the soy fed mice did better than expected. There were clear differences in the health outcomes that warranted further investigation.

With funding from the Waikato Medical Research Foundation, we will characterise the cytokine profile that have been induced in the mice. Thereby, gain an understanding of the processes that are being induced by the two different diets. This project will provide new scientific knowledge to support the claim that soy protein has benefits for IBD patients.

Abstracts of 2009 Grant Recipients

Does adrenaline co-administration with lipid based resuscitation in bupivacaine induced cardiac arrest alter return of spontaneous circulation?

Dr Martyn Harvey

Local anaesthetic drugs are commonly employed to provide regional anaesthesia for operative procedures. Inadvertent overdose with local anaesthetics however may result in cardiac arrest, from which successful resuscitation is rare. Intravenous infusion of lipid emulsion has been demonstrated to effect return of spontaneous circulation in animal and human subjects suffering local anaesthetic induced circulatory collapse. Lipid has additionally proven beneficial in animal models of toxicity secondary to a number of non local anaesthetic drugs. Incorporation of lipid emulsion into general clinical practice however requires examination of outcome when co-administered with commonly employed resuscitation drugs.

Dr Harvey is investigating the role of intravenous lipid emulsion in amelioration of drug induced cardiac toxicity. Bupivacaine is a commonly utilised local anaesthetic drug which may result in cardiac arrest when administered in excess. Resuscitative measures, in bupivacaine induced cardiac arrest, routinely includes administration of adrenaline. The purpose of which is to increase cardiac perfusion during CPR. Incorporation of lipid emulsion into resuscitation guidelines for local anaesthetic overdose has gained widespread acceptance, with animal models demonstrating superior outcome to CPR and adrenaline alone. However, no studies exist examining administration of lipid emulsion and adrenaline in concert.

The purpose of this study is to explore the effect of adrenaline co-administered with lipid emulsion in bupivacaine induced cardiac arrest. In an established bupivacaine induced cardiac arrest model, resuscitation outcome will be compared when incremental dose adrenaline is co-administered with lipid emulsion. The results will be employed to guide clinical recommendation for patients suffering cardiac arrest secondary to overdose with this, and other similar agents.

Abstracts of 2009 Grant Recipients

Testing the effect of temperature and polyethylene glycol on neocortical slice viability

Dr Logan Voss

Abstract

The isolated neocortical slice preparation is a technique that utilises slices of brain tissue that are maintained alive in artificial solution resembling the normal brain environment. The preparation can be used to test the effect of drugs and different conditions on tissue activity. It is used extensively in neuroscience research because of the ability to rigidly control tissue conditions. Temperature is one such variable, however there is ongoing debate about the optimum temperature for running the slice preparation. Anecdotally slice viability and health is said to be reduced at higher temperatures (e.g. 36°'a1C). For this reason many laboratories choose to maintain slices at room temperature, sacrificing the benefit of keeping the tissue closer to physiological conditions (approx 36°'a1C). To our knowledge, the effect of temperature on neocortical slice viability has not been systematically studied. The main aim of this study therefore, is to quantify the effect of temperature on neocortical slice tissue viability. This will be done using two fluorescence stains that stain specifically for live and dead cells, respectively.

The effect of temperature on the ratio of live/dead stain will be correlated. The results from this study will add important information to the ongoing debate on the optimum temperature for running cortical slice experiments. This work also has clinical significance because of the importance of brain cooling in protecting against ischaemic and traumatic brain injury. To extend this work, we will investigate the effect of a putative brain protection compound, polyethylene glycol (PEG). PEG has been shown to have neuro-regenerative properties, but its effect on isolated neocortical tissue has not been investigated. Using the same live/dead stain, we will correlate the effect of PEG on slice viability at different temperatures. If PEG is shown to limit brain damage, further animal experiments will be planned looking at the correlation between PEGs of different molecular weights and brain protection. This work could lead on to clinical trials.

Abstracts of 2009 Grant Recipients

Hearts and Minds: Physical health indicators in chronic mental illness

Dr David Menkes

Abstract

Metabolic syndrome, a combination of central obesity, high blood pressure, and abnormalities in blood sugar and fat, constitutes an important set of risk factors for cardiovascular disease and premature death. Patients with chronic mental illness, and especially those treated with antipsychotic drugs (APDs) are known to be at increased risk of metabolic syndrome. In light of the problem being common and readily identifiable, standards for monitoring such individuals have been developed. Metabolic syndrome is, however, yet to be consistently monitored or effectively managed by health services in NZ and elsewhere. Maori and other Polynesians are known to have elevated baseline rates of metabolic syndrome , but the effect of ethnicity in combination with APD treatment is yet to be established.

In order to study and begin to address this problem, we have identified 700 adult psychiatric patients in Hamilton, approximately 30-40% Maori, currently prescribed APDs. With the support of two Waikato Clinical School undergraduate summer studentships (2007-8 and 2008-9), we developed methodology for recruitment and monitoring of this group. By March 2009 we had collected complete data from 84/112 participants, 23 of whom identified as Maori and 61 as European New Zealander (Pakeha). The overwhelming majority 77/84 (92%) of completers met at least 1/5 standard (ATP-III) criteria for metabolic syndrome . Three or more criteria, thought to indicate clinical significance, were found in 19/23 (83%) of Maori and 27/61 (44%) of Pakeha participants. This result indicates a highly significant (Odds ratio 5.98, p=0.0016) excess of metabolic syndrome among APD-treated Maori.

Since only one third of our participants with metabolic syndrome were receiving medical treatment for any feature of the syndrome, these results indicate an urgent unmet health need, particularly among Maori. This finding must be considered tentative, given our small sample size, particularly of Maori. As we have learned from the study thus far, a number of barriers to effective monitoring of metabolic syndrome in APD-treated patients also complicate research recruitment. The priority now is to extend our recruitment, particularly of Maori, to enable a more comprehensive and informative data analysis. To do this we will seek institutional permission and ethical approval to recruit participants from services with a high concentration of Maori, notably Hauora Waikato and regional forensic services. In addition to confirmation of the effect of ethnicity, we intend to explore the contribution of gender, age, and duration of antipsychotic exposure. Future extensions of this study, currently being planned but beyond the scope this proposal, will identify a comparison sample of Waikato Maori never exposed to APDs.

Astracts of 2009 Grant Recipients

Phase II Trial of Peri-Operative Cimetidine in Early Colorectal Cancer

Dr Michael Jameson

Abstract

Cancer of the large bowel was the most common cancer in NZ in 2003. Despite appropriate surgery, chemotherapy and radiotherapy, only about 60% of patients will survive it. An ulcer-healing drug, cimetidine, has shown promising results in patients having surgery for this cancer. Cimetidine appears to keep the immune system functioning adequately after major surgery and takes away "landing sites" for cancer cells that escape into the bloodstream. This appears to prevent recurrence of bowel cancer, with about 30% more patients surviving in 4 small clinical trials.

A large trial involving over 1000 patients is needed to prove the benefits of cimetidine in patients having surgery for early bowel cancer. However, before undertaking this large trial, we need to clearly define how long we need to give patients cimetidine to have the optimal effect and how to reliably identify patients most likely to benefit from it. In addition we wish to demonstrate that we can recruit patients in sufficient numbers that we are confident that we can initiate a major phase III trial with NZ hospitals making a major contribution.

We've planned this clinical trial to address these questions, recruiting 60 patients having surgery for early bowel cancer at Waikato Hospital. They will take either cimetidine or "dummy" tablets twice daily starting a week before the operation and continuing for 4 weeks afterwards. We will take blood tests over 5 weeks, do special testing on patients' tumours and will also see if patients have fewer problems, such as wound infections, after surgery.

Abstracts of 2009 Grant Recipients

Volumetric and Growth Factor Assessments of Negative Pressure Wound Therapy

TM Vasudevan, N. Chiang

Abstract Background

Skin ulcers of the lower legs can be debilitating for patients and can be a burden on our health system caring for these patients. Topical negative pressure (TNP) therapy has seen a paradigm shift in wound management and is increasingly popular in wound care setting over the past decade. Although widely used, its evidence on benefits and mechanisms is limited and non-conclusive. Larger randomised controlled studies are demanded to demonstrate its benefits over traditional wound dressings.

Aim

We aim to provide objective evidence that TNP therapy enhances wound healing. This study targets wound healing by measuring wound volume over time between TNP therapy and traditional wound dressings.

We also study the mechanisms of TNP therapy at a tissue and molecular level. We aim to investigate the balance between the promoting growth factors for wound healing and inhibitory cytokines; as well as tissue oxygenation around the wound.

Design

Prospective randomised controlled trial will be conducted in the vascular surgical unit to test the hypothesis that TNP therapy is more effective than traditional dressings in terms of wound healing rate. This will be measured by wound volumes over time.

The mechanisms of TNP therapy will also be interrogated by evaluating the changes in the balance between growth factors that promote healing and inhibitory cytokines in the wound environment. Microvascular circulation at the wound will also be investigated between the groups postulating that TNP therapy enhances tissue oxygenation and subsequently wound healing.

Subjects

64 patients with an ulcer or a wound in the lower legs that is suitable for TNP therapy will be recruited and allocated randomly to one of two groups.

Treatment group – TNP therapy Control group – Traditional wound dressings.

Main Outcome Measures

The primary endpoint is wound volume reduction at 2 weeks. Secondary endpoints include analyses of growth factor, cytokines, tissue oxygenation and time to complete healing.

Health Outcomes and Impact

Positive outcome will demonstrate that TNP therapy does have a role in our health system in managing foot ulcers. It will reveal the efficacy and effects of TNP therapy at a tissue and molecular level. This scientific evidence looking at growth factors and tissue oxygenation is not known in previous human studies. This will benefit the community worldwide and other surgical specialties, especially plastic surgery.

Funding Allocation

This grant will enable the purchase of Silhouette Mobile by ARANZ Medical, which is a device that measures the volume of the wound objectively and accurately. The remaining funding will contribute to the analysis of growth factors between TNP therapy and traditional dressings.

Abstracts of 2009 Grant Recipients

Tissue Oxygenation and Wound Healing in Vascular Surgery

N Chiang, TM Vasudevan, J Sleigh, L Plank

Abstract

Background

Poor wound healing and failure to salvage a patient's limb as a result of unsuccessful revascularisation are the "banes of a vascular surgeon's life". Evaluating methods to reduce these risks will have significant impact in our practice, especially for high-risk vascular patients.

My PhD comprises various studies that primarily target wound healing and tissue oxygenation. Wound healing is measured quantitatively using a surrogate biochemical marker to collagen deposition called hydroxyproline- a method that is validated worldwide. Analyses of growth factors and their mRNA will also be performed and is essential to investigate the wound environment at a molecular level.

There is, as yet, no gold standard in evaluating tissue oxygenation. Ankle-brachial Index (ABI) and toe-brachial index (TBI) are widely used in the practice of vascular surgery. However, it has its limitations on providing oxygenation measures around the wound and inadequate with calcified vessels.

Transcutaneous oxygenation measurement (TCOM) system uses a heated transducer that is placed around the region of interest to detect oxygen levels of the tissue around the electrode. It has been validated in predicting wound healing, successful vascular reconstruction and amputation levels.

A novel tissue oxygenation measurement system using hyperspectral technology (HTCOM) was developed in 2006, called OxyVu™'aa. It offers a different option which provides detailed 'oxygen anatomy' around the area of interest and is more sophisticated. This machine was bought into the unit in December 2008.

The preliminary validation study for OxyVu™'aa did not show a significant correlation between TCOM and HTCOM. In this study, single readings at the first metatarsal joint were compared.

The grant funded five TCOM machines and one replacement TCOM electrode for my completion of PhD. The extra machines will enable simultaneous recordings of the area of interest and a reference point. This reference point is crucial to provide an index that is a more accurate measurement of tissue oxygenation.

The machines are key members to the studies in my PhD which include:

- Further validation of OxyVu™'aa with ABI, TBI and TCOM in vascular patients with severe arterial insufficiency.
- Ilomedin on Tissue Oxygenation in End-Stage Limb Ischaemia.
- The effects of supplemental peri-operative oxygen, extended peri-operative warming and peri-operative Ilomedin (a prostacyclin analogue) on wound healing, tissue oxygenation and patient outcome in infra-inguinal surgery.

The benefit of my PhD is of two folds. It provides objective evidence that simple conservative methods can improve tissue oxygenation and wound healing in vascular surgery at a tissue and molecular level, thus reducing patients' morbidity by improving tissue viability. It also provides information about OxyVu™'aa, which has been voted as the best innovation in 2008 in Podiatry Care, and how this relates to TCOM ABI and TBI.

Abstracts of 2009 Grant Recipients

The Sugar Babies Study

A randomised controlled trial

Deborah Harris

Overview

Hypoglycaemia (low blood sugar level) is the only common preventable cause of brain damage in babies. It is most common in the first twenty-four hours after birth, and is a frequent reason for admission to the Newborn Intensive Care Unit. Admission to the Newborn Intensive Care Unit separates mother and baby, and can interrupt the establishment of breast feeding.

Oral carbohydrate (sugar) is the first line of treatment for the conscious hypoglycaemic diabetic patient. Waikato Hospital is the only hospital in Australasia to use oral 40% dextrose (sugar) gel for treatment of low blood sugar levels in babies. However, there is no reliable evidence about whether this treatment does more good than harm. We plan to undertake a study to determine the benefits and risks of this treatment in hypoglycaemic newborn babies.

Glucose concentrations are routinely measured in newborn babies by intermittent blood tests, usually one to four hourly. However, blood glucose concentrations are known to fluctuate following birth and therefore periods of hypoglycaemia may be missed. We have recently developed experience with continuous interstitial glucose monitoring in the newborn. We have found continuous glucose monitoring to be reliable, well tolerated and easy to use in newborn babies.

In November 2008, we began the Sugar Babies Study; a randomised placebo-controlled trial of the use of oral dextrose gel for management of neonatal hypoglycaemia. Term and near-term babies at high risk of developing low blood sugar concentrations are recruited before or shortly after birth, and undergo continuous glucose monitoring as well as routine blood glucose monitoring. If the baby develops hypoglycaemia during the first 48 hours after birth, they are randomised to receive either oral 40% dextrose gel or an identical placebo gel. The primary objective of the study is to assess the effectiveness of the gel in reversing low blood glucose concentrations. We will also look at other possible effects and side effects of the treatment, including the length of time taken to reverse the hypoglycaemia, the effect on the incidence of admission to the neonatal intensive care unit, the effect on the baby's feeding and successful breast feeding, and the mother's feelings about having a baby in a study.

Significance and expected benefits

Hypoglycaemia is very common soon after birth , and is the most common cause of preventable brain damage in the newborn. The diagnosis and management remain controversial. Many babies are admitted to the Newborn Intensive Care Unit for treatment. We hope to determine the effectiveness of a simple oral treatment that may reverse hypoglycaemia and allow the mother and baby to remain together. This may improve the rate of breast feeding and decrease hospital costs. In addition, we aim to determine whether our current regime for intermittent blood glucose monitoring can be improved.

Waikato Medical Research Foundation (Inc)

Financial Statements

For the year ended 31 May 2009

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Waikato Medical Research Foundation (Inc)

Statement of Financial Position
As at 31 May 2009

	2009 $	2008 $
Accumulated Funds	**1,256,666**	1,240,545
Represented by:		
Current Assets		
Westpac	**30,733**	14,393
ASB	**51,311**	436
	82,044	14,829
Investments		
Cash and Equivalents	**173,046**	211,861
NZ Fixed Interest	**968,291**	852,337
NZ Listed Property	**61,414**	89,574
Australian Investments	**43,753**	58,075
American Investments	**8,827**	13,061
British Investments	**1,495**	5,495
	1,256,826	1,230,403
Total Assets	**1,338,870**	1,245,232
Current Liabilities		
Accounts Payable	**82,204**	4,687
Net assets	**$1,256,666**	$1,240,545

N.C. Karalus
3/7/09

N Karalus
Chairman

R Baird
3/7/09

R Baird
Treasurer

STAPLES RODWAY Marked for Identification Purposes

Waikato Medical Research Foundation (Inc)

Statement of Movements in Equity
For the year ended 31 May 2009

	2009 $	2008 $
Accumulated Funds		
Opening balance as at 1st June 2008	**1,240,545**	1,301,577
Plus: Net Surplus/(deficit)	**16,121**	(61,032)
Closing Balance as at 31st May 2009	**$1,256,666**	$1,240,545

Waikato Medical Research Foundation (Inc)

Statement of Financial Performance
For the year ended 31 May 2009

	Note	2009 $	2008 $
Income			
Dividends		**10,494**	9,637
Donations	3	**38,877**	15,075
Foreign exchange gain		**2,508**	-
Grant - Trust Waikato		**65,000**	65,000
Interest		**79,427**	80,367
Income on realisation of investments		**827**	14,364
		197,133	184,443
Expenditure			
Administration expenses including website		**13,374**	11,556
Advertising and promotion expenses		**3,919**	1,918
Audit fee		**2,250**	2,447
Fees paid to auditor for other services		**5,267**	5,012
Foreign exchange loss		**-**	9,695
Grants	2	**115,516**	165,000
Loss on realisation of investments		**-**	1,904
Portfolio management fees		**5,074**	5,368
Unrealised loss on investments		**35,612**	42,575
		181,012	245,475
Net surplus/(deficit)		**$16,121**	($61,032)

Waikato Medical Research Foundation (Inc)

Statement of Cash Flows
For the year ended 31 May 2009

	2009 $	2008 $
Cash Flows from Fund Raising Activities		
Receipts from donations and grants	**103,877**	80,075
Less Fundraising expenses	**(3,919)**	(1,918)
Net cash flow from fund raising activities	**99,958**	78,157
Cash Flows from Investing Activities		
Receipts from dividends and interest	**89,921**	90,004
Plus Sale of investments	**389,358**	291,405
Less Investments made	**(448,057)**	(259,482)
Less Portfolio Management fees	**(5,074)**	(5,368)
Net cash flow from investing activities	**26,148**	116,559
Cash Flows from Research Activities		
Grants made	**(38,000)**	(185,000)
Administration and audit fees	**(20,89)**	(20,302)
Grants refunded	-	-
Net cash flow from research activities	**(58,891)**	(205,302)
Net increase/(decrease) in cash held	**67,215**	(10,586)
Add Opening cash brought forward	**14,829**	25,415
Ending cash carried forward	**82,044**	14,829
Cash balances in statement of financial position	**$82,044**	$14,829

Waikato Medical Research Foundation (Inc)

Notes to the Financial Statements
For the year ended 31 May 2009

1. Statement of Accounting Policies

Reporting Entity
Waikato Medical Research Foundation is a non profit organisation registered under the Incorporated Societies Act 1908.

General Accounting Principles
The general accounting principles recognised as appropriate for the measurement and reporting of income and financial position on an historical cost basis, except for valuation of investments, have been consistently followed by the Foundation. Accrual accounting has been used to match revenue and expenses.

Particular Accounting Policies
The following particular accounting policies which materially affect the measurement of income and the financial position have been applied.

Investments
Investments are valued at market value in NZ dollars. Any increases/(decreases) in fair value are recognised in the statement of financial performance.

Revenue
Revenue is recognised in the statement of financial performance when the irrevocable right to receive the revenue is established.

Income Tax
The Waikato Medical Research Foundation (Inc) has been approved for legal charitable status and has obtained from the Inland Revenue Department an exemption for income tax. The Waikato Medical Research Foundation (Inc) is also a registered charity with the Charities Commission.

Differential Reporting
The Society qualifies for differential reporting because of it's size and nature. The Society has taken advantage of all available differential reporting exemptions, except in that it has produced a Statement of Cashflows.

Changes in Accounting Policies
There have been no changes in accounting policies since the previous annual financial statements.

Waikato Medical Research Foundation (Inc)

Notes to the Financial Statements Continued
For the year ended 31 May 2009

2. Grants Made

	2009 $	2008 $
N Chiang	**4,000**	-
G Devlin	-	17,653
S Finch	-	18,500
D Harris	**23,000**	-
P Harris	-	24,500
M Harvey	**13,350**	3,720
A Hodgkinson	**15,000**	-
M Jameson	**17,166**	-
L Leow	-	28,500
D Menkes	**15,000**	23,850
J Sleigh	-	30,000
E Tan	-	18,277
T Vasudevan	**6,000**	-
L Voss	**22,000**	-
	$115,516	$165,000

3. Donations

Cancer Society	**18,277**	15,000
Braemar Charitable Trust	**7,000**	-
F & S Clements	**5,000**	-
Estate of J Grace	**5,000**	-
Dr A T Rogers	**2,000**	-
A & D Lee	**1,000**	-
General	**600**	75
	$38,877	$15,075

4. Commitments and Contingencies

At balance date there are no known contingent liabilities. (2008: Nil)

At balance date there are no known capital commitments. (2008: Nil)

5. Related Parties

Professional fees are paid to Staples Rodway Waikato LP whom Rosanna Baird is a Director. There were no amounts owing as at 31 May 2009.

STAPLES RODWAY
dynamic financial answers

Audit Report
To the Members of Waikato Medical Research Foundation (Inc)

We have audited the financial report on pages 20 to 25. The financial report provides information about the past financial performance of the Foundation and its financial position as at 31 May 2009. This information is stated in accordance with the accounting policies set out on page 24.

Trustees' Responsibilities
The Trustees are responsible for the preparation of a financial report which fairly reflects the financial position of the Foundation as at 31 May 2009 and the results of operations and cash flows for the year ended on that date.

Auditor's Responsibilities
It is our responsibility to express an independent opinion on the financial report presented by the Trustees.

Basis of Opinion
An audit includes examining, on a test basis, evidence relevant to the amounts and disclosures in the financial report. It also includes assessing:

- the significant estimates and judgements made by the Trustees in the preparation of the financial report; and
- whether the accounting policies are appropriate to the Foundation's circumstances, consistently applied and adequately disclosed.

We conducted our audit in accordance with New Zealand Auditing Standards. We planned and performed our audit so as to obtain all the information and explanations which we considered necessary in order to provide us with sufficient evidence to obtain reasonable assurance that the financial report is free from material misstatements, whether caused by fraud or error. In forming our opinion we also evaluated the overall adequacy of the presentation of information in the financial report.

Other than in our capacity as auditor we have provided bookkeeping and accounting services to the Foundation.

Unqualified Opinion

We have obtained all the information and explanations we have required.

In our opinion the financial report on pages 20 to 25 fairly reflects the financial position of the Foundation as at 31 May 2009 and the results of its operations and cash flows for the year ended on that date.

Our audit was completed on 7 July 2009 and our unqualified opinion is expressed as at that date.

Staples Rodway

STAPLES RODWAY
Hamilton

WMRF Donors

Foundation Members

A H Franks
ANZ Bank
Baxter Healthcare
Sir John Logan Campbell
Gallagher Electronics
Glaxo Ltd
J M & J A Grace Family Trust
Norah Howell Trust
J R McKenzie Trust
Maurice & Phyllis Paykel Trust
Pharmaco NZ Ltd
Ready Mixed Concrete
Mrs A. Sanford
Trigon Packaging Systems
Trust Bank Waikato Ltd
Waikato Hospital Centennial

Major Donors

D V Bryant Trust
Cancer Society
Estate D J Carter
Cassel Trust Hospital
Mr Lyndon Clements
Donny Charitable Trust
Eastside Real Estate
E B Firth Charitable Trust
B & J Flower Trust
Elaine Hammond
P J Holman Family Trust
Mrs Annette Meade
Merck Sharp
Mobil Oils NZ
Nat Mutual Life
NZ Breweries
NZ Med Assn
Dr Amanda Oakley
Perry Foundation
Perry Holdings Ltd
Riker Laboratories
Roche Products Ltd
Rotary Club of Frankton
Soutar Trust
The Page Trust
Trust Waikato
Mr P J Vela
M J Waddington
J H & K S Wake
Estate Valerie Esther Worth
V E Worth

Life Members

3M Pharmaceuticals Ltd
Abbott Laboratories Ltd
Adam Molenaar Trust
B Adams
Mr J E Allen
Mr C D Arcus
Cynthia Armstrong
Mr R B Armstrong
Mrs Heather M Bailey
Dr Mercia Barnes
Mr Warwick Baskmore
Mr W T Billings
A & I Bojesen-Trepka Family Trust
Alan & Gillian Campbell
Mr Fergus Campbell
Dr G D Campbell
Dr L Chan
Dr Richard Clark
Mr Clive Cleland
Mr P W Crabb
Mr & Mrs M.C. Day
Mr K W Dey
Mrs A Dingle
Mr Robert Dobson
M & L Dunshea Family Trust
Dr J D Earwaker
Dr T C Fraser
Dr N R Freeman
WE & AM Fullerton
I M & RV Glenn
Mrs Jenepher Glenn
Glenn Family Trust
E Griffin
Dr A J Haslam
Dr Jack Havill
Mr Ron Hemi
T G & M E Hodgson
Mr John Hogan
Dr C H Hooker
Mr David Hoskin
Invitrogen Life Technologies
Mr Robert A Janes
Mr D Johnstone
Dr Steve Jones
Mr & Mrs G.S. Judd
Judd Family Trust
Dr Noel Karalus
Mr Geoff Laugeson
Dr R G Lawrence
Mr J G Macaulay
Dr D G McInnes
Mr Ken MacKay
Sir Duncan McMullin
Neil & Sonya Meltzer
Mr J Mortimer
Parker Davies Pty Ltd
Dr R G Pirrit
Mr R Rimmington
Dr K L Robertson
Mr L S Robinson
Mrs Frances Robinson
PR & SJ Rose
Dr RPG Rothwell
Mr A J Seeley
HT & MP Spencer
Mr Dryden Spring
Dr I B Sutton
Mr E A Taylor
Dr B E Tomlinson
Visique Rose Optometrists
Dr R B Waddington
Mr E L Waters
Dr RE Wright St Clair
Dr G Wynne-Jones
Dr B Herries Young

2008 / 2009 Donations received:

Mrs JR Allen

Braemar Charitable Trust

Alan and Gillian Campbell

Cancer Society – Waikato-Bay of Plenty Division

Finlay and Susan Clements

Mrs Jenepher Glenn

Estate of J. Grace

Mr A.J. Haslam

Anne and David Lee

Dr AT Rogers

Donation Form

I wish to make a donation to the
Waikato Medical Research Foundation

Please tick one

- ○ $50 ○ $100 ○ $200
- ○ $500 ○ $1000 ○ $2000
- ○ Other (Amount $ _____)
- ○ I enclose a cheque made out to : Waikato Medical Research Foundation
- ○ Please send me a receipt

As we are registered with the Charities Commission, all donations to Waikato Medical Research Foundation over $5.00 are tax rebatable.

Name of Donor _____

Address _____

_____

_____

Daytime Telephone _____

Post to:

Waikato Medical Research Foundation
Peter Rothwell Academic Centre
Private Bag 3200
Hamilton 3240

Telephone (07) 839 8750 Fax (07) 839 8712

Website: www.wmrf.org.nz