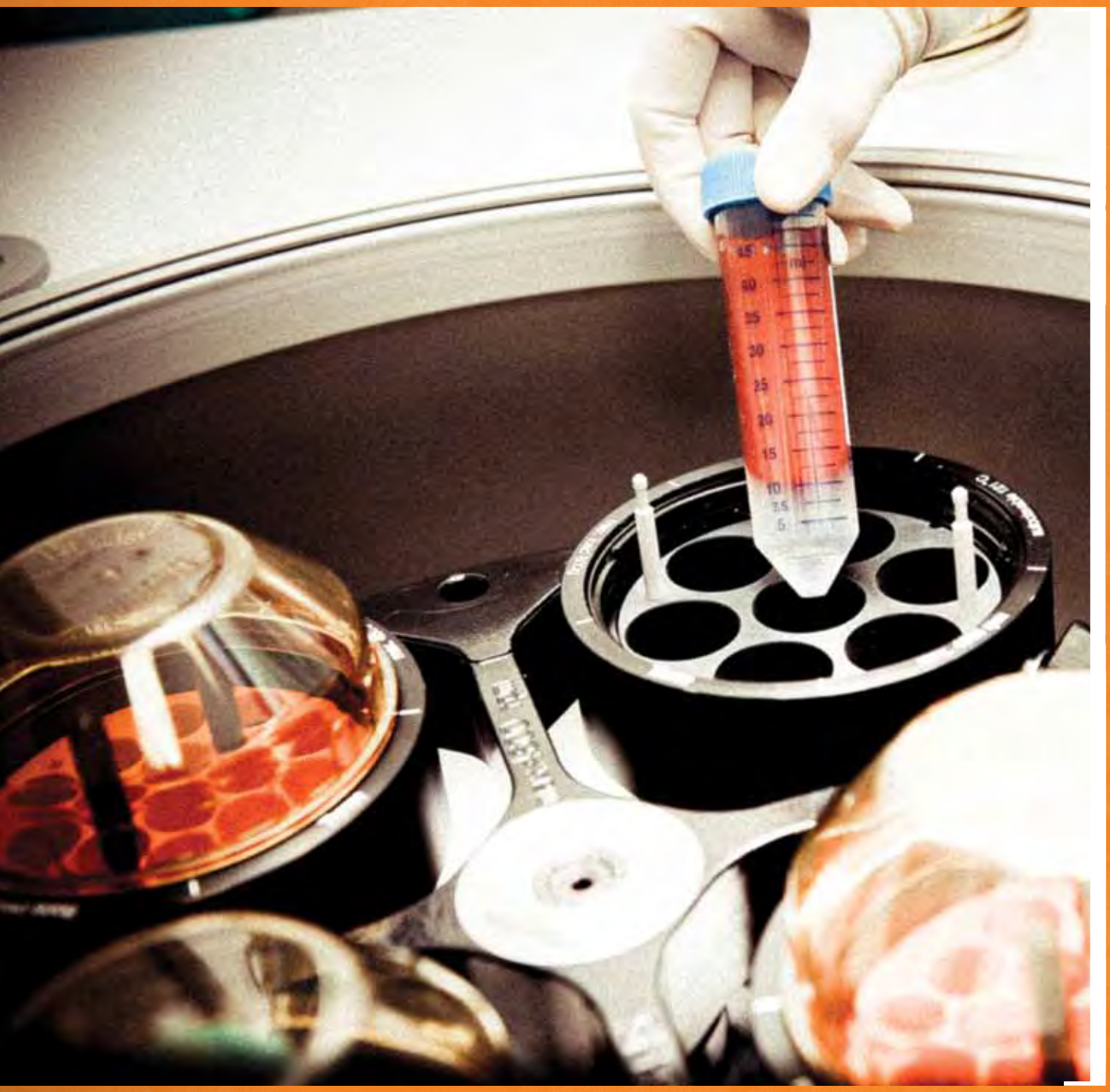
Annual Report

2011 | 2012

MALAGHAN INSTITUTE OF MEDICAL RESEARCH



This Annual Report covers the period 1 August 2011 – 31 July 2012

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The Malaghan Institute exists to make a difference in people's lives, and our scientists believe that the key to making this difference lies in harnessing the immune system, the body's own natural defence against disease.

Malaghan Institute Staff, 2012.

About Us

The Malaghan Institute is New Zealand's leading independent medical research institute, with a proud history spanning over three decades.

Our work is recognised internationally and our pioneering research programmes are focused on finding better treatments and cures for diseases affecting New Zealanders – including cancer, asthma and allergy, arthritis, MS and infectious disease.

In addition to our drive for making medical discoveries that impact health, the Malaghan Institute is committed to the education and support of New Zealand scientists and clinicians. Our reputation as a cutting-edge medical research and training facility sees us housing New Zealand's brightest and most creative scientists, doctoral students and post-doctoral fellows.

Our purpose-built facility on the Kelburn campus of Victoria University of Wellington is home to over 75 researchers and support staff. We also maintain close collaborative relationships with Universities, Crown Research Institutes, hospitals and clinics throughout New Zealand and overseas. Working with worldwide organisations ensures that our scientists keep abreast of the latest developments in the international arena, thus maintaining our research at a world-class level.

We are a registered charity and to ensure that the vital research at the Institute continues, we rely on contestable grants, corporate sponsorship, trusts, bequests and donations. All funding contributes to the world-changing potential we strive for, and the belief that we will find, and actually make available the cure for diseases affecting New Zealanders.

Chairman's Report

The enormous scientific and funding challenges faced by the Trustees, Director and staff continued in 2012, and gives all involved with the Institute the opportunity to solve, achieve and enjoy the very real progress which is being made.

The Director's report covers many of the most notable achievements of the Institute for the year. One of the most significant from the Board's perspective was the Science Review, the second we have done, to ensure that the research work of the scientific teams is both relevant and worthy of support, and that it can deliver meaningful contributions to New Zealand and the international community.

I am pleased to report that the review found the Institute has strong innovative programmes that deserve support and have the potential to considerably advance human health. The review team pointed to the difficulties faced by our research teams in maintaining international competitiveness in what is a very difficult New Zealand funding environment, and as a consequence the Board agreed to establish three Fellowships for our Group Leaders. These provide significant salary support, have a five year tenure and are funded from the income of the Capital Endowment Fund.

I am often asked how the Institute is funded. It is significant that a little over 60% of our funds are obtained by our researchers from competitive, taxpayer funded sources, managed by the Health Research Council and the Royal Society's Marsden Fund. Other grants are sought from private funders, including the Cancer Society, the Wellington Medical Research Foundation and many others. We are also fortunate to have many individuals, Trusts and corporates who donate and fund our efforts, along with the activities of our Friends groups with their events and golf days.

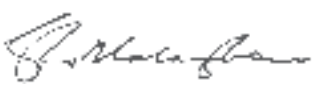
The Institute is governed by the Trust Board who meet quarterly; and the Executive Committee, which comprises myself, Bryan Johnson and Graham Le Gros, who meet regularly throughout the year. I would also like to acknowledge the commitment and efforts of Dan Williams, who Chairs the Audit and Finance, and Investment Committees and also Matthew Malaghan, who gives focus to our promotional activities through his role as Chair of the Development Committee. These committees involve both Trustees and senior staff.

During the year we had several visits from Parliamentary representatives. The visit by the Hon. Stephen Joyce as Minister of the new Ministry of Business, Innovation and Employment (MBIE) was especially important as we seek to enhance the work of our allergic diseases, food allergy and gut health research programmes. This work establishes another solid platform to join that of our cancer related work.

The Institute, whilst continuing to extend and develop its relationships and collaborations within New Zealand, is continuing to nurture its international connections. On a home perspective, our base here at the Victoria University of Wellington campus remains a strong supportive rock for all our endeavours.

On a final note my thanks as always to my fellow Trustees, the Research teams and Executive of the Institute; and you our supporters, Friends and cheerleaders.

We are looking forward to another busy year with progress being sought on all fronts.



Mr Graham Malaghan ONZM FCILT
CHAIRMAN

Director's Report

It is a privilege to work in research. To be in a position of creating opportunities which could make a difference to people's lives is something none of us here at the Malaghan Institute take for granted.

Having said this, it is getting tougher each year to fund research. There is less government money coming to basic research and the available grants are being broken up into smaller amounts to spread it as fairly as possible amongst all the dedicated researchers in this country. The only way to survive in the current climate is to try and do even more, so as an Institute we have set our staff very high goals.

One of these goals is to focus on getting our key basic research discoveries through preclinical development and into patients – something Associate Professor Ian Hermans, the newly appointed Malaghan Institute Deputy Director of Research, is making great strides towards with his cancer vaccine research. This year Assoc Prof Hermans' research team completed a phase I glioblastoma multiforme (GBM) vaccine clinical trial, the outcomes from which will be published later this year. I am happy to report that as a result of the continued generosity of Ian Paterson and family from Just Paterson Real Estate, this work will continue, building upon the clinical trial and Mr Martin Hunn's promising basic GBM research.

Preparations are now underway for a melanoma vaccine trial, central to which is Dr Olivier Gasser, who we welcomed from Europe in August last year. We are very grateful to the Thompson Family Foundation for their support in resourcing our melanoma vaccine programme, which has enabled Dr Gasser to undertake essential scientific studies in the lead-up to the clinical trial.

To be successful you must work with the best and we are very fortunate in this regard. I would like to congratulate Trustees Graham Malaghan and David Mossman on their respective Queen's Birthday Honours; Dr Bridget Stocker on her Royal Society of Chemistry Easterfield Medal and Manhire Prize for Creative Science Writing; Dr Elizabeth Forbes-Blom on her promotion to Senior Research Fellow, supporting our translational allergy work; and acknowledge my own Wellingtonian of the Year Award, which I feel reflected the efforts and support of so many of you reading this.

I would like to finish by farewelling one of our research stars, Dr Joanna Kirman, who left the Institute to take up a senior lectureship at the University of Otago. We will miss Jo's insight on many issues but acknowledge this is an important step up in her research career and wish her all the best for the future.

For two weeks this year, as a nation, we tuned into the Olympics and enjoyed seeing our top athletes achieve success. Science is just as competitive an arena - requiring years of dedication, training and discipline - but it is publications in prestigious journals such as Science and Nature that are the 'gold medals' we strive for. With the backing of our hardworking Trust Board and Friends Groups, the generosity of our supporters and unwavering passion and commitment of our staff, I feel the Institute is well placed to patiently pursue its core agenda and in doing so, achieve great scientific success.

Prof Graham Le Gros FRSNZ
DIRECTOR

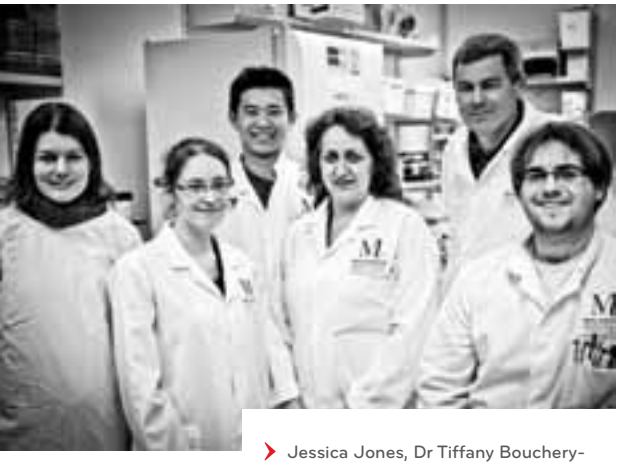
› Kylie Price.

Research

The Malaghan Institute holds a special and distinctive place in the New Zealand health research sector.

Our scientists specialise in the fields of cellular immunology, haematology, cellular and molecular biology, carbohydrate chemistry, immune models of human disease and the development of immunotherapies and vaccines.

Our goal is to deliver medical research discoveries that provide tangible health benefits to the community.



Jessica Jones, Dr Tiffany Bouchery-Smith, Sotaro Ochiai, Mali Camberis, Prof Graham Le Gros, Ryan Kyle.

Research Group

Allergic & Parasitic Diseases

RESEARCH INTERESTS

Prof Graham Le Gros' Allergic and Parasitic Diseases Research Group is currently working on developing an immunotherapy or vaccine that specifically shuts down the allergic immune response, and the relationship to immunity to parasitic diseases.

Understanding the signals that trigger the initiation of asthma and allergy is critical for the identification of specific treatments that selectively suppress the allergic Th2 immune response. Prof Le Gros' research group is using murine models, immunological assays and structure/function analyses to generate much needed information in this poorly understood field. Important outcomes of this work will be the development of generally applicable vaccines and therapies for the treatment of individuals with established disease, and the identification of improved immunological markers for monitoring human airway inflammation and allergy.

The Th2 immune response normally functions to protect individuals from parasitic worm infections. The Allergic and Parasitic Diseases Research Group are therefore applying their knowledge of the allergic immune response to the development of a vaccine against human hookworm, one of the great neglected tropical diseases that infects one billion people globally. Using the rodent model of human hookworm, *Nippostrongylus brasiliensis*, in combination with cytokine and cell knockout murine models, they are looking for putative targets both for vaccine design and testing of vaccine efficacy in the field.

HIGHLIGHT

In November 2011, Prof Graham Le Gros won the Science and Technology category of the 2011 Wellingtonian of the Year Awards, in recognition of the quality allergy and parasitic disease research he is pioneering here at the Malaghan Institute.

RESEARCH GROUP MEMBERS

Group Leader:
Prof Graham Le Gros BSc(Massey), Dip Immunol(Otago), MPhil(Auckland), PhD(Auckland), FRSNZ – Director of Research

Visiting Scientists:
Prof Manfred Kopf from Molecular Biomedicine Institute of Integrative Biology, ETH Zurich, Dr Gavin Painter from Industrial Research Limited and Dr Irene Salinas from the National Institute of Water and Atmospheric Research

Senior Research Fellow:
Dr Elizabeth Forbes-Blom BSc(VUW), PhD(ANU)

Research Fellow:
Dr Tiffany Bouchery-Smith MSc(Rennes), PhD(MNHN, Paris)

Senior Research Officers:
Mali Camberis BSc(VUW), Jessica Jones BSc(Melbourne), Melanie Prout BSc(Hons)(VUW), Shiau-Choot Tang Grad Dip Sci(VUW)

Research Officer:
Catherine Plunkett BBmedSc(Hons)(VUW) (to Feb 2012)

PhD Students:
Ryan Kyle BBmedSc(Hons)(VUW), Helen Mearns BSc(Hons), MSc(Cape Town, RSA), Sotaro Ochiai BSc(Hons (Auckland), Catherine Plunkett BBmedSc(Hons)(VUW) (from Mar 2012), Marcus Robinson BBmedSc, MSc(Hons)(VUW)

Summer Students:
Giovanna Le Gros, Richard Portch

RESEARCH FUNDING

AgResearch Ltd • Fonterra Co-operative Group Ltd • Foundation for Research, Science & Technology • Health Research Council of New Zealand • Industrial Research Ltd • Rex & Betty Coker Foundation • Springhill Charitable Trust & Frimley Foundation • The Dr Marjorie Barclay Trust

Research Group

Arthritis & Inflammation

RESEARCH INTERESTS

Uric acid exists in the body in both soluble and crystalline forms and it is generally believed that elevation of serum uric acid is a marker of inflammation. The Arthritis & Inflammation Research Group, led by Dr Jacquie Harper, is looking at how the crystalline and soluble forms of uric acid impact on immune regulation and inflammatory disease.

Gout is an intensely painful form of arthritis affecting a great number of New Zealanders. An attack of acute gout is triggered by the formation of uric acid (MSU) crystals, causing rapid and painful joint inflammation. Research from Dr Harper's team places mononuclear phagocytes center stage as key orchestrators of this inflammatory response.

The Arthritis & Inflammation Group is looking at the inflammatory functions of recruited monocytes during the immune response *in vivo*, to determine whether they are driving or resolving inflammation, or both. This work includes understanding how central obesity and hyperuricemia, which are key risk factors for gout, alter the innate inflammatory response to MSU crystals.

They are also investigating the effects of the soluble form of uric acid on human immune cell function in both a clinical and basic research setting. The goal of this work is to determine if soluble uric acid alone exerts effects on immune cell inflammatory responses that are unrelated to MSU crystal formation.

In collaboration with Plant & Food Research, Dr Harper's research team is investigating ways in which fruit consumption may be used to alleviate or moderate inflammation. Inflammatory-related allergic conditions such as asthma and eczema are currently treated with steroids that have long-term complications. Here, allergic lung inflammation (asthma) is being used as a test model to identify fruit preparations capable of suppressing inflammatory cell infiltration and chronic lung damage.

Collectively these studies are providing important insights into new potential therapeutic options for the improved management of inflammatory diseases. They are also serving to enhance our understanding and appreciation of the multi-level interactions between the innate and adaptive immune systems.

Rene McLaughlin, Stefanie Steiger, Odette Shaw, Dr Jacquie Harper, Lisa Shaw.

RESEARCH FUNDING

Arthritis New Zealand • Foundation for Research, Science & Technology • Health Research Council of New Zealand • New Zealand Lottery Grants Board • The Estate of WJ Thomson • Wellington Medical Research Foundation

RESEARCH GROUP MEMBERS

Group Leader:
Dr Jacquie Harper BSc(Hons), PhD(Otago)

Research Fellow:
Dr Shujie He MSc, PhD, MBChB(Jilin, China)

Senior Research Officer:
Odette Shaw BSc(Hons)(Otago)

Research Officer:
Lisa Shaw BSc, MSc(Otago)

PhD Students:
Rene McLaughlin BBmedSc(Hons) (VUW), Blake Paget BBmedSc(Hons) (Auckland), Stefanie Steiger DipSci(MLU, Germany)

Research Group

Cancer Cell & Molecular Biology

Prof Mike Berridge, Alanna Cameron, An Tan, Dr James Baty, Dr Patries Herst, Carole Grasso.

RESEARCH INTERESTS

The main focus of Prof Mike Berridge's Cancer Cell & Molecular Biology research programme is to apply new knowledge and technologies to the treatment of human diseases, with a particular emphasis on cancer and diseases involving altered energy metabolism.

The Malaghan Institute is a world leader in developing safe vaccination strategies for treating cancer and is trialling these in late stage melanoma and glioblastoma patients. Recently, highly targeted melanoma drugs against the mutant BRAF oncogene have shown dramatic early effects in the clinic and have been approved for human use. Nevertheless, drug-resistant tumour cells persist, leading to recurrence.

The Cancer Cell & Molecular Biology Research Group is investigating conditions under which immunotherapy can be combined with highly targeted melanoma drugs with the aim of improving patient outcome. They have also developed models of childhood brain tumours and are working to improve treatment of these cancers through vaccination.

Prof Berridge's research team is also investigating intercellular mitochondrial trafficking in health and disease. Using mitochondrial genome knockout melanoma and breast cancer models that exhibit long lag periods to tumour growth, they have shown that tumour growth is dependent on acquisition of mitochondrially-encoded genes from the tumour microenvironment. This 'transforming' event also facilitates metastasis to the lung and is best explained by mitochondrial transfer between cells via membrane nanotubes, a phenomenon previously described *in vitro*.

To further investigate the role of intercellular mitochondrial transfer in health and disease, they have initiated a collaboration to build a synthetic mitochondrial genome encoding genetic markers that will then be transfected into tumour cells, progenitor cells and eventually, embryonic stem cells depleted of their mitochondrial genome, to generate mice with fluorescently-labelled mitochondria. This new technology will be applied not only to tumour biology but also to the mitochondriopathies, to degenerative muscle, brain and cardiovascular disease, and to normal and ageing physiology.

RESEARCH GROUP MEMBERS

Research Group Leader:
Prof Mike Berridge BSc, MSc(Hons), PhD(Auckland)

Research Fellows:
Dr James Baty BSc(Hons)(VUW), PhD(Otago), An Tan BSc(VUW)

Visiting Scientist:
Dr Patries Herst BSc, MSc(Nijmegen, Netherlands), MPhil(Waikato), PhD(Otago) from the Department of Radiation Therapy, University of Otago, Wellington

Research Officer:
Carole Grasso BSc(Hons) (West of England)

Masters Student:
Alanna Cameron BBmedSc(VUW)

RESEARCH FUNDING

Cancer Society of New Zealand (National Body and Wellington Division) • Child Health Research Foundation • Genesis Oncology Trust • Melanoma Research Alliance • New Zealand LAM Trust/LAM Australasia Research Alliance • Wellington Medical Research Foundation

Research Group

Cell Survival

RESEARCH INTERESTS

The primary focus of Dr Melanie McConnell's Cell Survival Research Group is to understand how cancer cells survive stress, and to apply this knowledge to the development of effective cancer therapies.

Cancer cells have to survive free radicals, lack of oxygen, reduced nutrients, immune attack and changes in metabolism. During chemotherapy and radiation treatment of cancer patients, cancers are subjected to further stress. Despite this, some cells survive and cause relapse and metastasis. This is thought to be due to the presence of cancer stem cells, which are drug and radiation resistant.

Dr McConnell's research team has established various methods to isolate, identify and characterise cancer stem cells using cell culture, human tumour culture, flow cytometry, real-time RT-PCR and immunofluorescence microscopy. They have mouse models of brain tumours to study the properties of self-renewal, therapy resistance and metastasis in whole organisms. The stress response and cellular survival pathways activated in cancer cells are related to the cell phenotype and to patient survival.

In other work the Cell Survival Research Group is looking at how the same cellular survival pathways can be used to best advantage in diseases where accelerated cell death occurs, such as motor neurone disease.

RESEARCH GROUP MEMBERS

Group Leader:
Dr Melanie McConnell BSc(Hons), PhD(Otago)

Visiting Scientist:
Dr Patries Herst BSc, MSc(Nijmegen, The Netherlands), MPhil(Waikato), PhD(Otago) from the Department of Radiation Therapy, University of Otago, Wellington

Research Officers:
Leticia Castro BMedSci(Hons)(Sydney), Marie-Sophie Fabre MSc(Brest), Carole Grasso BSc(Hons)(West of England), Xiaowen Yu BBmedSc(Hons)(VUW)

Masters Students:
Susanna Brow BSc, BBmedSc(VUW), Jonathan Brown BSc(VUW)

Honours Student:
Nicole Jones BBmedSc(VUW)

Summer Student:
Daphne Cohen BSc(Hons)(Auckland)

RESEARCH FUNDING

Cancer Society of New Zealand (National Body) • Genesis Oncology Trust • Maurice Wilkins Centre for Molecular Biodiscovery • The Estates of Ellen, Sinclair, Barbara and Alison Wallace • University of Otago • Wellington Medical Research Foundation

Nicole Jones, Dr Melanie McConnell, Dr Patries Herst, Leticia Castro, Jonathan Brown, Marie-Sophie Fabre, Carole Grasso, Susanna Brow.

Research Group

Immune Cell Biology

RESEARCH GROUP MEMBERS

Group Leader:
Prof Franca Ronchese PhD(Padua), Dip Microbiology

Research Fellows:
Dr Lisa Connor BBmedSc(Hons), PhD(Otago), Dr Shujie He MSc, PhD, MBChB(Jilin, China)

Senior Research Officers:
Evelyn Hyde MSc(Distinc)(Otago), Dr Jianping Yang BM(Shanxi)

PhD Students:
Naomi Baker BMLSc(Otago), Sabine Kuhn Diplom Biologie(LMU Munich, Germany)

Masters Students:
Kerry Hilligan BBmedSc(VUW), Sonai Lim BBmedSc(VUW)

Summer Student:
Courtenay O'Sullivan

Prof Franca Ronchese, Naomi Baker, Kerry Hilligan, Evelyn Hyde, Dr Jianping Yang, Dr Lisa Connor, Dr Shujie He.

RESEARCH INTERESTS

The primary research interest of Prof Franca Ronchese's Immune Cell Biology Research Group is dendritic cells - specialised immune cells that can process environmental cues into signals that activate or switch off immune responses. Dendritic cells are found in most tissues in the body, but differ in specific activation requirements and properties.

Dendritic cells are ideal targets for the development of immunotherapies for diseases such as cancer, where a more powerful immune activation might result in the control of tumour growth; or allergy and autoimmune disease, where dendritic cells play an important role in local inflammation.

Prof Ronchese's research team collaborates with other groups in Wellington and overseas to address the following questions:

- Can dendritic cells in tumours be manipulated to support an intratumoral environment that favours tumour rejection, and minimises immune suppression?
- What are the weapons that immune cells require to successfully attack cancer?
- What signals instruct dendritic cells to initiate allergic immune responses?
- Can dendritic cells be targeted to specifically reduce allergic inflammation with minimal effects on other immune responses?

RESEARCH FUNDING

Foundation for Research, Science & Technology • Health Research Council of New Zealand • New Zealand Lottery Grants Board • Rotary Club of Wellington • Wellington Medical Research Foundation

Research Group

Immunoglycomics

RESEARCH INTERESTS

The goal of Dr Bridget Stocker's Immunoglycomics Research Group is to understand the role of carbohydrates in immune responses, and to apply this knowledge to the development of more effective therapies for diseases such as asthma, cancer and tuberculosis.

In the same way that genomics and proteomics have fuelled discoveries in all biological sciences, immunoglycomics, the unravelling of the role of glycoconjugates in immune processes, is now thought to be an emerging research field that will generate significant new scientific knowledge.

Although it is known that glycoconjugates play critical roles in cellular events, such as cell signalling, bacterial and viral infection, and the metastasis of tumour cells, detailed knowledge about the identity and mode of action of the glycoconjugates involved is lacking. To better understand the role of glycoconjugates in biology, the Immunoglycomics Research Group uses the latest synthetic methodology, including recently developed novel 'protecting-group-free' strategies, to gain access to unique molecular probes and tools that can then be used to understand the role of specific immune cells and enzymes in disease.

These studies will provide the first detailed insight into how carbohydrate structures can influence the immune system and the knowledge gained will be used to aid in the diagnosis and treatment of disease.

HIGHLIGHT

In November 2011, Dr Bridget Stocker was awarded the Royal Society of Chemistry Easterfield Medal, in recognition of her quality and original chemistry research. She also won the fiction category of the Royal Society of New Zealand Manhire Prize for Creative Science Writing.

RESEARCH FUNDING

Cancer Society of New Zealand (National Body and Wellington Division) • Genesis Oncology Trust • Health Research Council of New Zealand • New Zealand Lottery Grants Board • The Royal Society of New Zealand Marsden Fund ·• Wellington Medical Research Foundation

RESEARCH GROUP MEMBERS

Group Leader:
Dr Bridget Stocker BSc(Hons, 1st class), PhD(VUW)

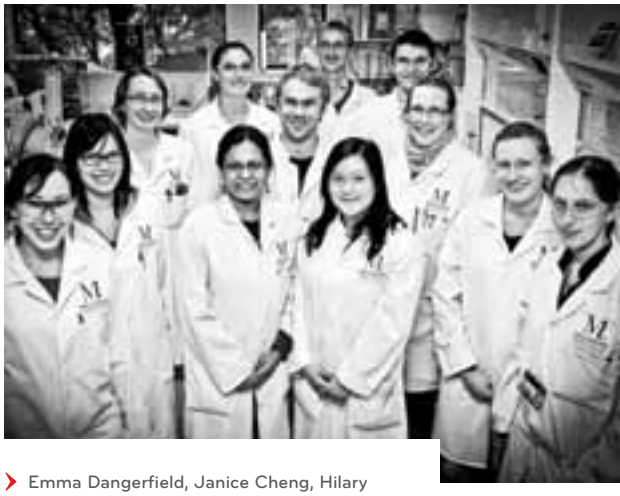
Co-Group Leader:
Dr Mattie Timmer (VUW) MSc, PhD(Leiden, The Netherlands)

Research Officer:
Stephanie Chee BSc(VUW)

PhD Students:
Janice Cheng BBmedSc(Hons) (VUW), Hilary Corkran BSc(Hons) (Massey), Emma Dangerfield BBmedSc(Hons)(VUW), Ashna Khan BSc(USP, Fiji), PGDip(Auckland), Gert-Jan Moggré MSc(Netherlands), Stefan Munneke BSc, MSc(Netherlands), Janelle Sauvageau BSc, MSc(UL, Canada), Anna Win-Mason BSc(Hons)(VUW)

Masters Students:
Jessie Bird BBmedSc(VUW), Amy Foster BBmedSc(VUW)

Visiting Masters Student:
Selma Eising BSc(Groningen, The Netherlands)



Emma Dangerfield, Janice Cheng, Hilary Corkran, Dr Bridget Stocker, Ashna Khan, Stefan Munneke, Dr Mattie Timmer, Stephanie Chee, Gert-Jan Moggré, Anna Win-Mason, Amy Foster, Janelle Sauvageau.

Research Group

Infectious Diseases

RESEARCH GROUP MEMBERS

Group Leader:
Dr Joanna Kirman BSc(Hons), PhD(Otago) – WMRF Malaghan Haematology Fellow

Senior Research Officer:
Fenella Rich BSc(Hons), DPH(Distinc)(Otago)

Research Officer:
Clare Burn BSc(Hons)(Otago)

PhD Students:
Lindsay Ancelet BSc(Hons)(USask, Canada), MSc(Toronto, Canada), Kelly Prendergast BBmedSc (Hons)(VUW)

Masters Student:
Cornelia Walker DipHumanBiol(Philipps, Germany)

Honours Student:
Ramakrishna Gopalakrishnan BTech(Anna, Chennai, India)

Kelly Prendergast, Lindsay Ancelet.

RESEARCH INTERESTS

In May 2012, Dr Joanna Kirman relocated her research programme to the University of Otago, Dunedin. Although this move marked the end of the Malaghan Institute's Infectious Diseases Research Group, Dr Kirman will continue to collaborate with our Group Leaders on several ongoing research projects.

The major focus of Dr Kirman's infectious diseases research is to reduce the incidence of tuberculosis (TB) in New Zealand through the development and implementation of more effective TB vaccines.

TB kills more people worldwide than any other bacterial disease and highly lethal outbreaks of extensively drug resistant forms of the bacteria have highlighted the need for more effective therapies. The only long-term solution to controlling the spread of TB is through vaccination, however the current TB vaccine, BCG, fails to reliably protect against adult TB lung disease.

The Infectious Diseases Research Group is using well-established laboratory models of TB to identify the key cytokines and cell types responsible for mediating immunity against *Mycobacterium tuberculosis* for the development of new vaccines.

In other work Dr Kirman and colleagues are involved in an international collaborative study with Dr Tristram Ingham from the Wellington Asthma Research Group, University of Otago, Wellington. The purpose of this study is to understand why New Zealand children, particularly Maori and Pacific infants, are more likely to develop severe lower respiratory tract infections and require hospitalisation.

RESEARCH FUNDING

Health Research Council of New Zealand • Maurice Wilkins Centre for Molecular Biodiscovery • New Zealand Lottery Grants Board • Wellington Medical Research Foundation

Research Group

Multiple Sclerosis

RESEARCH INTERESTS

Our Multiple Sclerosis research programme is headed by Dr Anne La Flamme, an Associate Professor at Victoria University of Wellington's School of Biological Sciences.

Dr La Flamme's primary research interest is in the immune regulation of disease. In particular, her work focuses on the pivotal role of one specific immune cell, the macrophage, in the regulation of pro-inflammatory diseases such as multiple sclerosis (MS).

Macrophages are multifunctional immune cells and are key mediators of inflammatory immune processes. Dr La Flamme's research group has shown that treatments that alter a macrophage's state of activation, and thus alter the immune 'climate', can prevent central nervous system inflammation and progressive paralysis in a murine model of human MS. Additionally, Dr La Flamme and colleagues are investigating if these treatments or other immune factors can regulate microglia (brain-resident macrophages) function in the brain.

Identification of the disease-inhibiting pathway(s) by which these macrophage-altering treatments prevent disease may uncover much-needed therapeutic targets to inhibit or reduce the severity of MS.

In complementary studies, Dr La Flamme's research group is also collaborating with other New Zealand and international researchers, to identify alternative drugs for treating MS.

Dr Anne La Flamme.

RESEARCH GROUP MEMBERS

Dr La Flamme's research group is based at the School of Biological Sciences, Victoria University of Wellington

Research Associate:
Dr Anne La Flamme BS(MIT), MS, PhD(Washington)

RESEARCH FUNDING

The Great New Zealand Trek Charitable Trust Inc •
The Neurological Foundation of New Zealand

Research Group

Vaccine Research

Dr Olivier Gasser, Evelyn Bauer, Ching-Wen Tang, Collin Brooks, Assoc Prof Ian Hermans, Astrid Authier, Cameron Field, Sara McKee, John Gibbins, Taryn Osmond, Brigitta Mester.

RESEARCH INTERESTS

The overall goal of Associate Professor Ian Hermans' Vaccine Research Group is to design more effective vaccines against diseases such as cancer. It is known that white blood cells called T cells can kill tumour cells. Vaccines that induce the activity of T cells therefore hold considerable promise as new therapeutic agents.

Assoc Prof Hermans' research team is looking at the specific immune cell populations involved in eliciting effective immune responses to vaccination, including the dendritic cells responsible for stimulating T cells, and other less well-known cells such as Natural Killer T (NKT) cells that contribute to the induced response. Working together with chemists, they are aiming to define compounds that can be incorporated into vaccines to ensure optimum, coordinated activity of all of the immune cells involved.

They are also exploring how other therapies for cancer, such as chemotherapy, radiation and hyperthermia, affect the immune system, with a view to combining these therapies with vaccination.

The Vaccine Research Group works closely with New Zealand leaders in the fields of immunology, medicinal chemistry and clinical oncology to test their vaccines in cancer patients.

RESEARCH FUNDING

Cancer Society of New Zealand (National Body and Wellington Division) • Foundation for Research, Science & Technology • Health Research Council of New Zealand • Industrial Research Limited • Just Paterson Real Estate • The Estate of Isabel Mary Tucker • The Graham Hall Bequest • The Royal Society of New Zealand Marsden Fund • The Thompson Family Foundation, Inc. • University of Otago • Wade Thompson • Wellington Medical Research Foundation

RESEARCH GROUP MEMBERS

Group Leader:
Assoc Prof Ian Hermans BSc(Hons)(Otago), MSc(Distinc)(Otago), PhD(VUW) – Deputy Director of Research

Senior Research Fellows:
Dr Olivier Gasser MSc(Strasbourg), PhD(Basel), Dr Troels Petersen MSc, PhD(Copenhagen)

Clinical Research Fellows:
Mr Martin Hunn MBChB(Otago), FRACS, Dr Robert Weinkove MA(Cantab), MBBS(London), MRCP(UK), FRCPath(UK)

Visiting Scientist:
Collin Brooks from the Centre for Public Health Research, Massey University

Clinical Trials Manager:
Evelyn Bauer NZCSc, Cert Animal Sci & Tech(Massey)

GMP Research Assistant:
Brigitta Mester MSc(Hungary)

Research Nurse:
Catherine Wood RN, BN, MHSc

Senior Research Officers:
Astrid Authier BSc, MSc(Massey), Kathryn Farrand MSc(Massey)

Research Officer:
Ching-Wen Tang MSc(Otago)

PhD Students:
Cameron Field BSc(Hons)(Otago), John Gibbins BBmedSc(Hons)(VUW), Taryn Osmond BBmedSc(Hons)(VUW), Dianne Sika-Paotonu BSc, BBmedSc, MBmedSc(Hons)(VUW)

Visiting PhD Student:
Sara McKee BSc(Hons)(Otago) from the University of Otago

Honours Student:
Tram Nguyen BBmedSc(VUW)

Rene McLaughlin.

Cancer

Despite revolutionary advances in medicine over the past two centuries, cancer treatment has progressed slowly and many cancers still cannot be effectively treated. The toxicity of some current cancer treatments also represents a considerable part of the health burden of the disease itself. New targeted therapies with limited toxicity are needed to increase survival with a good quality of life.

Therapies that activate the immune system (immunotherapies) have the potential to eliminate cancer cells from the body. For decades, patients have been given bone marrow transplants to drive immune responses against cancer tissue, but this can be a blunt tool that is often associated with toxicity to healthy tissues.

We now know that the immune system can be programmed to target cancer cells more precisely through the use of specific vaccines. Cells of the immune system that are triggered in this way have powerful cancer-killing capability and can move around the body to eliminate tumours that have spread to other tissues. What's more, the immune cells retain a 'memory' for cancer; so can re-launch an attack should the cancer cells start to grow again.

Cancer vaccines can be created from a patient's own tumour cells, or from synthetic components made to look like a tumour. The aim is to make the tumour appear dangerous to the body in the same way that an infectious bacterium or virus would, leading to a strong immune response.

A good basic understanding of the immune system has meant that we can now exploit the key cellular and molecular interactions required to specifically induce cancer-killing cells. The Malaghan Institute is at the forefront of this research with an established international track record going back more than

Cancer affects one in three New Zealanders, either personally or through a family member or friend. It is the leading cause of death in this country.

16 years. We are continually improving our own vaccine technology through basic research in the laboratory, and have conducted our own clinical trials of different forms of the vaccine in cancer patients.

Supporting these studies are basic research projects investigating conditions under which immunotherapy can be combined with highly targeted cancer drugs to improve the outcomes of patients with melanoma or glioblastoma multiforme. Our scientists are also designing and synthesising novel glycolipid adjuvants to enhance vaccine-induced anti-tumour immune responses.

In recent years there has been a new focus on the cancer stem cell, or tumour initiating cell, and the identification of ways to target immunotherapies against these drug and radiation resistant cancer cells. Through research aimed at increasing our knowledge of the basic biology of cancer stem cells and the pathways they use to survive chemotherapy and radiotherapy treatments, our scientists hope to develop safe and effective ways to eradicate them.

By combining the disciplines of immunology, cell biology and drug discovery in translational research programmes that involve immunologists, biochemists, molecular biologists, chemists and clinicians, we believe our research has the potential to launch a new era in cancer treatment.

WHY NEW ZEALAND NEEDS THIS RESEARCH

Every day in New Zealand approximately 51 people are diagnosed with cancer and 22 will die from the disease.[1] Many patients diagnosed with terminal cancer are understandably keen to participate in clinical trials of novel treatments, even if their legacy is to simply help others in the future, rather than benefit themselves.

We believe that cancer vaccine-based immunotherapy has the potential to make a real difference to the lives of individuals and families affected by cancer. Our research has shown that we can use vaccines to programme the immune system to launch an attack on growing tumours.

In contrast to chemotherapy and radiotherapy, this form of cancer treatment is well tolerated with few side effects.

We have the expertise to make cancer vaccines here at the Malaghan Institute. Through our close working relationship with clinicians from Wellington Hospital and the Wellington Blood and Cancer Centre, we are able to administer the vaccines to patients enrolled in our clinical trials. Importantly, we have the supporting infrastructure and research capability required to push the field forward.

Any improvement to patient outcome through our efforts would not only improve the nation's health, but could also have significant economic benefits with international opportunities.

[1] Cancer Society of New Zealand.

› Alanna Cameron.

CLINICAL HIGHLIGHT

Glioblastoma multiforme (GBM) is a highly aggressive brain tumour. The standard treatments for GBM are surgery, radiotherapy and chemotherapy, however the tumour is highly radiation and drug resistant, making it ultimately fatal. Capital & Coast District Health Board Neurosurgeon Mr Martin Hunn and Malaghan Institute Vaccine Research Group Leader Assoc Prof Ian Hermans, hypothesised that by acting through entirely different mechanisms, immunotherapy might combine effectively with chemotherapy in attacking GBM tumour cells.

Earlier this year they completed a phase I clinical trial in patients whose tumours had recurred after standard treatment. The aim was to test whether it is feasible and safe to combine chemotherapy with immunotherapy. The custom-made vaccines used in the trial were created from dendritic cells isolated from the patient's blood, and tissue from their surgically removed tumour. The results of the trial are currently being analysed and prepared for publication, but early indications are that the combination treatment is safe, and could slow tumour growth in some patients.

In conjunction with the clinical trial, Mr Hunn has been undertaking some basic research to explore the possibility of simplifying the GBM vaccine.

"My laboratory-based experiments with cell-free vaccines that contain tumour tissue and an immune-stimulating adjuvant, have shown anti-tumour activity," says Mr Hunn. "This is an important development because some patients enrolled in the GBM trial were unable to be vaccinated, simply because we couldn't isolate enough dendritic cells to make their vaccine."

By removing the need for dendritic cells, Mr Hunn believes this new vaccine strategy will make the therapy more accessible to patients. M

By bringing together New Zealand's best clinical and scientific expertise, this research has the potential to make a real difference to the lives of individuals and families affected by cancer.

RESEARCH HIGHLIGHT

USING VITAMIN C TO BOOST RADIATION THERAPY

In radiation therapy a lethal dose of radiation is delivered to a tumour whilst sparing the surrounding healthy tissues as much as possible. Radiation kills both normal and cancerous cells by generating free radicals that destroy their DNA, however healthy cells have repair mechanisms that enable them to recover from the treatment more quickly.

"High dose vitamin C also generates free radicals in the acidic, metal-rich environment of a tumour, but not in normal tissues," says Dr Patries Herst, a senior lecturer in Radiation Therapy at the University of Otago, Wellington. "We therefore hypothesised that high dose vitamin C might work synergistically with radiation treatment to increase free radical damage to resistant tumours such as glioblastoma multiforme (GBM)."

In collaboration with Dr Melanie McConnell, Dr Herst investigated the effect of combining high dose vitamin C with radiation on the survival of cancer cells isolated from GBM tumours. They found that pre-treating GBM cells with vitamin C did indeed make it easier to kill them with radiation.

"The use of high dose vitamin C as an anti-cancer treatment is very controversial," says Dr Herst. "Early studies using oral and intravenous vitamin C showed a survival benefit for terminally ill patients but later studies using only oral vitamin C did not."

"However, if carefully designed clinical trials support our basic research findings that combining high dose vitamin C with radiation therapy improves patient survival, there may be merit in combining both treatments for radiation-resistant cancers such as GBM." M

Herst PM, Broadley KW, Harper JL, McConnell MJ (2012) Pharmacological concentrations of ascorbate radiosensitize glioblastoma multiforme primary cells by increasing oxidative DNA damage and inhibiting G2/M arrest. Free Radic Biol Med, 52:1486-93

RESEARCH HIGHLIGHT

HUNTING FOR THE ELUSIVE BREAST CANCER STEM CELL

Breast cancers, like most tumours, consist of mixed populations of cells with varying morphology and metastatic ability. The cancer stem cell hypothesis posits that while the majority of cancer cells have a limited lifespan, a sub-population is able to form new tumours due to the acquisition of self-renewal activity. These cancer stem cells (CSC) have been shown to be inherently resistant to conventional cancer treatments.

After the first identification of CSC in leukaemia, markers that can selectively identify CSC from other tumour types have been actively sought, to facilitate their direct targeting with novel drug or immune-based therapies.

In murine breast cancer models, CSC activity has been associated with the protein Sca-1. As a precursor to a breast cancer immunotherapy trial, Dr Melanie McConnell, Prof Mike Berridge and colleagues investigated the utility of using the progenitor cell protein Sca-1, either naturally expressed or induced, as a mouse breast CSC marker.

"We found that Sca-1 cells isolated directly from murine breast cancer cells did not have CSC activity," says Dr McConnell. "Even when Sca-1 was turned up in every cell by growth in stem cell media, there was no CSC activity."

"Surprisingly Sca-1 induction actually led to less CSC activity, particularly metastasis," she says. "This was shown to be due to loss of TGFB2 and SMAD2 expression."

"Our results reinforce prior work, by ourselves and by others, that functional assays rather than marker expression are critical for CSC analysis." M

Matilainen H, Yu XW, Tang CW, Berridge MV, McConnell MJ (2012) Sphere formation reverses the metastatic and cancer stem cell phenotype of the murine mammary tumour 4T1, independently of the putative cancer stem cell marker Sca-1. Cancer Lett, 323:20-8

RESEARCH HIGHLIGHT

A CANCER VACCINE MADE FROM VIRUS-LIKE PARTICLES AND α-GALACTOSYLCERAMIDE

Assoc Prof Ian Hermans' Vaccine Research Group has shown previously that the stimulatory glycolipid α-galactosylceramide (α-GalCer) can be used to enhance immune responses to dendritic cell vaccines. In recent collaborative research undertaken with Prof Vernon Ward and Dr Sarah Young from the University of Otago, the ability of α-GalCer to also enhance the function of vaccines made from 'virus-like particles' was examined.

Virus-like particles contain the outer shell of a virus, but no genetic material. This means that while they are able to provoke an immune response to their structures, they are incapable of infectious spread.

Prof Ward and Dr Young's research has shown that virus-like particles developed from rabbit hemorrhagic disease can be used to deliver antigens to the appropriate cells in the body, to stimulate specific immune responses. However injection of the particles alone was insufficiently stimulatory to generate the signals required to initiate immune responses capable of eliminating tumours. One of Dr Young's PhD students, Sara McKee, visited the Malaghan Institute for 18 months to determine whether combining the particles with α-GalCer improved the strength of the anti-tumour immune responses elicited by the vaccine.

"Sara showed that α-GalCer can bind directly to the virus-like particles, enabling simple vaccines to be manufactured," says Assoc Prof Hermans. "Importantly, vaccines created in this way exhibited extremely potent anti-tumour activity *in vivo*, promoting the activation of T cells and antibody production."

The broad immunity elicited by the α-GalCer coated particles makes the vaccines highly useful for medicine and agriculture - various applications of which are currently being explored.

McKee SJ, Young VL, Clow F, Hayman CM, Baird MA, Hermans IF, Young SL, Ward VK (2012) Virus-like particles and α-galactosylceramide form a self-adjuvanting composite particle that elicits anti-tumor responses. J Control Release, 159:338-45

RESEARCH HIGHLIGHT

HOW MYCOBACTERIA COULD HELP TREAT CANCER

Tumour immunotherapy with mycobacteria and their cell wall components has been used with varying degrees of success to treat melanoma and leukaemia, as well as bladder, colon and lung cancers. These treatments stem from Dr William Coley's early investigations in the late 1800s, which were based on the hypothesis that the immune responses elicited by bacteria are equally capable of destroying tumour tissue.

In research published in the journal *Cancer Immunology, Immunotherapy,* Dr Joanna Kirman, Prof Franca Ronchese and colleagues describe how they applied 21st century technology to tease out the scientific basis for the anti-tumour effects observed with this age-old cancer therapy.

In support of previous findings, they found that when *Mycobacterium smegmatis* - a fast-growing non-pathogenic relative of TB - was given adjacent to a thymoma tumour, the rate of growth of the tumour slowed dramatically.

"Interestingly when we looked in the lymph nodes near to where *M. smegmatis* was given, we could detect a special type of antigen presenting cell that wasn't present in the absence of mycobacterial treatment," says Dr Kirman. "We think these cells might be important for driving the anti-tumour response."

This is the first time these inflammatory immune cells have been observed in context of mycobacterial immunotherapy, so Dr Kirman, Prof Ronchese and their teams plan to do further work to determine if, and how, these cells induce robust T cell mediated anti-tumour immune responses.

This knowledge will facilitate the identification of improved ways to harness the impressive immune-stimulating properties of mycobacteria for the treatment of cancer.

Rich FJ, Kuhn S, Hyde EJ, Harper JL, Ronchese F, Kirman JR Induction of T cell responses and recruitment of an inflammatory dendritic cell subset following tumor immunotherapy with *Mycobacterium smegmatis*. Cancer Immunol Immunother, (in press)

Hilary Corkran.

Marcus Robinson, Dr Elizabeth Forbes-Blom, Prof Graham Le Gros.

Asthma & Allergy

The prevalence of allergic disease in this country is amongst the highest in the world, with one in five New Zealanders affected by asthma, food allergy, eczema or hay fever.

Allergic diseases are caused by an overreaction of the immune system to harmless environmental triggers that we breathe in, touch or eat. In fact it is only one specific part of the immune system that is activated – the Th2 immune response, which normally functions to protect us from parasitic worm infections.

We do not know why the immune systems of individuals with asthma or food allergy respond to pollen and food proteins as though they were parasites. However, the consequences of this mistaken identity can be severe, with sufferers experiencing swelling, vomiting, skin irritations and breathing difficulties as a result of their runaway immune responses.

Current treatments for allergic diseases rely on the use of non-specific immune suppressive agents such as corticosteroids, which can leave patients more susceptible to common infections such as influenza. With the aim of developing specific therapies and vaccines that selectively suppress the allergic Th2 immune response and potentially cure the patient, our scientists are using unique laboratory models of asthma and allergy to gain more detailed knowledge of the signals that initiate the allergic pathway.

The majority of our asthma and allergy research is undertaken in Prof Graham Le Gros' Allergic & Parasitic Diseases Research Group and Prof Franca Ronchese's Immune Cell Biology Research Group. Senior Research Fellow Dr Elizabeth Forbes-Blom specialises in the study of gut health and is currently developing novel food allergy sensitisation models to reveal, for the first time, the earliest cellular and molecular events that take place during the development of the allergic immune response in the gut. Other research Group Leaders involved in asthma and allergy research include Dr Bridget Stocker and Dr Jacquie Harper.

These investigations address important gaps in our current understanding of allergic disease and have clear applications for the development of immunotherapies and improved low-allergenic functional foods (such as infant formulas) for affected individuals.

Asthma, eczema and food allergies continue to increase throughout the world and are recognised as one of the emerging global health issues.

RESEARCH HIGHLIGHT

'PUNCHING' HOLES IN DENDRITIC CELLS – COULD THIS BE THE KEY TO CONTROLLING ASTHMA?

Specialised white blood cells called Th2 T cells are known to play an essential role in the pathogenesis of asthma. They remain resting until they are activated by immune cells called dendritic cells, in response to harmless environmental allergens such as house dust mites or pollen.

Previous work at the Malaghan Institute and other laboratories has shown that activating another class of T cells called cytotoxic T lymphocytes, or CTLs, could prevent the development of asthma in disease models. With the support of the Health Research Council of New Zealand, Dr Noriyuki Enomoto and Prof Franca Ronchese investigated this phenomenon further. They discovered that the ability of CTLs to stop airway inflammation was dependent on their release of a pore-forming protein called perforin.

"Our work has revealed a previously unappreciated mechanism for CTL regulation of the immune response, which may be relevant to the pathogenesis of allergic asthma," says Prof Ronchese. "We believe that activated CTLs can kill allergen-presenting dendritic cells in the airways by effectively 'punching' holes in them."

"With fewer dendritic cells around to activate the disease-mediating Th2 cells in the airways, there is consequently less allergic airway inflammation."

This work was undertaken using an acute model of allergic asthma. Prof Ronchese's research team is now developing a more clinically relevant chronic model of asthma to investigate the potential of exploiting CTL activity for the treatment of individuals with established disease.

Enomoto N, Hyde E, Ma JZ, Yang J, Forbes-Blom E, Delahunt B, Le Gros G, Ronchese F (2012) Allergen-specific CTL require perforin expression to suppress allergic airway inflammation. J Immunol, 188:1734-41

RESEARCH HIGHLIGHT

A 'FLU SHOT' FOR ASTHMA AND ALLERGY?

Every winter we are encouraged to get our annual flu shot, to forearm our immune system with all the information it needs to ward off potential influenza infections. Can the same principle can be applied to the prevention of asthma and allergy?

"What we are attempting to do here at the Malaghan Institute is develop an immunotherapy or vaccine that specifically shuts down the Th2 immune response," says Prof Graham Le Gros. "This is a more natural approach to treating allergic disease, because we are effectively using the immune system to do all the work. All we are doing is pointing it in the right direction."

While the availability of an over the counter vaccine or 'allergy shot' is still some time off, Prof Le Gros and Prof Franca Ronchese have made significant progress in the basic research underpinning the development of a vaccine.

"Recently we have shown how our immune system is able to generate responses that control each other," says Prof Ronchese. "We need to do more work to fully understand the implications of these results but they might help to explain why some people are more likely to become allergic than others."

By undertaking carefully constructed investigations using well-defined disease models, Malaghan Institute scientists believe they are on the right track to producing a viable treatment option for reversing New Zealand's asthma and allergy epidemic.

Ma JZ, Lim SN, Qin JS, Yang J, Enomoto N, Ruedl C, Ronchese F (2012) Murine $CD4^+$ T cell responses are inhibited by cytotoxic T cell-mediated killing of dendritic cells and are restored by antigen transfer. PloS One, 7:e37481

Arthritis & Inflammation

Changes in serum uric acid levels are a common feature of many human inflammatory diseases.

Odette Shaw.

Inflammation is a common underlying feature of numerous human diseases including arthritis. In New Zealand over half a million people will be affected by arthritis during their lifetime.

There are over 100 different types of arthritis, with the most common forms being osteoarthritis, rheumatoid arthritis and gout. Importantly, arthritis has no age restriction, with many conditions affecting the very young as well as the elderly. Often starting with acute inflammatory flares causing painful joint swelling, chronic inflammation in arthritis commonly leads to permanent joint damage, loss of joint function, mobility and chronic pain.

Inflammation in arthritic conditions is generally treated using non-steroidal anti-inflammatory drugs, but with variable success. The Arthritis & Inflammation Research Group led by Dr Jacquie Harper, is currently focused on understanding which key inflammatory processes could be targeted for improved arthritis management.

Recently there has been a significant escalation in inflammation-related conditions associated with the rise in obesity in developed countries. These conditions include Type II diabetes, cardiovascular disease and gouty arthritis - commonly grouped under the term 'metabolic syndrome'. A common feature of metabolic syndrome is the elevation of serum uric acid (hyperuricaemia), however whether hyperuricaemia is the cause or effect of these inflammatory conditions is undetermined. To unravel this mystery, Dr Harper's team is working with clinicians in Wellington, Auckland and Christchurch, to look at how treating hyperuricaemia impacts on inflammation.

Clinicians have access to a wide number of treatments for managing inflammation, however there is substantial evidence of the beneficial effects of diet in managing inappropriate inflammatory conditions such as asthma. Asthma affects over 20% of New Zealanders, therefore the ability to moderate lung inflammation and minimise the use of corticosteroids through diet would significantly impact on quality of life. Working together with Plant & Food Research, Dr Harper and colleagues are profiling the anti-inflammatory properties of New Zealand fruit crops to identify candidate fruits that could be utilised to alleviate lung inflammation in individuals with asthma.

RESEARCH HIGHLIGHT

IDENTIFICATION OF THE BRADYKININ RECEPTOR 2 AS A POTENTIAL THERAPEUTIC TARGET FOR GOUT

Acute gout is triggered by the deposition of monosodium urate (MSU) crystals in the joints, resulting in an influx of inflammatory immune cells. It is known that the initial phase of inflammatory cell recruitment occurs in response to the production of immune signalling proteins called chemokines at the site of inflammation. What isn't well understood however, is how and why inflammatory cells continue to be recruited long after chemokine production has ceased.

To address this question Dr Jacquie Harper and colleagues used their acute gout model to identify alternative pathways that could maintain cell recruitment, independent of chemokine production.

"We discovered that activation of the bradykinin receptor 2 (B2) on cells in the membrane was a key driver for ongoing immune cell recruitment in the absence of chemokine production," says Dr Harper.

"Our data also suggest that the B2 receptor plays an important functional role in maintaining membrane permeability."

"To our knowledge this is the first time that the B2 receptor has been shown to directly impact on acute MSU crystal-induced leukocyte infiltration and identify the receptor as a potential therapeutic target for managing gout."

Dr Harper and colleagues are now investigating in more detail the contribution of the cells in the membrane to the regulation of inflammatory cell migration in response to MSU crystal inflammation during a gout attack.

Shaw OM, Harper JL (2011) Bradykinin receptor 2 extends inflammatory cell recruitment in a model of acute gouty arthritis. Biochem Biophys Res Commun, 416:266-9

RESEARCH HIGHLIGHT

CONTROL OF MSU CRYSTAL-INDUCED INFLAMMATION BY RESIDENT AND STROMAL CELLS

Monocyte recruitment is a characteristic feature of the inflammatory immune response to MSU crystals in gout, however the specific cell population(s) responsible for initiating this event is unclear. Monocytes are drawn to sites of inflammation by the chemokine CCL2, so Dr Jacquie Harper and colleagues set out to identify which cells produced CCL2 in response to MSU crystal deposition.

"We discovered that rather than CCL2 coming initially from the resident immune cells, that it was in fact the cells in the membrane surrounding the inflammatory site that were responsible for the first wave of monocyte recruitment," says Dr Harper.

In summary, Dr Harper's research has shown that while MSU crystal-induced neutrophil recruitment is dependent on CXCL1 production by resident macrophages, monocyte infiltration appears to be primarily initiated by the release of low level CCL2 by stromal cells in the surrounding tissue. As such, the synovial tissue in the joint may play a direct role in regulating inflammation in gout.

Since monocyte recruitment plays such an important role in gouty inflammation, Dr Harper and colleagues are now investigating sources of CCL2 production in gout patients that could be contributing to monocyte trafficking during a gout attack.

Liu X, Chia E, Shaw OM, Martin WJ, Harper JL Rapid CCL2 release by membrane stromal cells initiates MSU crystal-induced monocyte recruitment in a peritoneal model of gouty inflammation. Eur J Inflamm, (in press)

Infectious Diseases

One billion people worldwide are infected with helminth parasites.

› The nematode parasite *Nippostrongylus brasiliensis*, a rodent model of human hookworm. These images are courtesy of Mali Camberis and Alfonso Schmidt.

Despite all its highly evolved mechanisms for identifying and fighting off the daily onslaught of bacteria, viruses, fungi and parasites, the immune system sometimes fails to provide the protection we need. For individuals living in areas where infectious diseases such as hookworm and tuberculosis (TB) flourish, the end result of a poorly equipped immune system can be devastating.

Hookworm is a leading cause of morbidity in developing countries, while TB claims a staggering 1.4 million lives and newly infects nearly nine million people every year, making it the leading cause of mortality by an infectious disease after HIV. Here in New Zealand, there are approximately 600 notifications of TB disease each year, with 300 new cases diagnosed.

Evidence of emerging drug resistance in hookworm control and highly lethal outbreaks of extensively drug-resistant TB, have highlighted the need for more effective therapies to control these diseases.

Both Prof Graham Le Gros and Dr Joanna Kirman – who has recently moved to the University of Otago – believe the only long-term solution to controlling infectious diseases such as hookworm and TB is through vaccination. Their respective research teams are using the rodent nematode parasite *Nippostrongylus brasiliensis* and murine models of TB, to learn more about the immune responses elicited by these infectious organisms. Complementing this research is a drug discovery platform involving Dr Bridget Stocker's Immunoglycomics Research Group.

The knowledge and technologies emerging from these research programmes will provide valuable insight into which cytokines and cells need to be targeted for the development of more effective treatments and vaccines for hookworm and TB, and other infectious diseases. M

Tuberculosis kills more people than any other bacterial disease.

RESEARCH HIGHLIGHT

WHY IT IS IMPORTANT TO CHOOSE THE RIGHT MODEL WHEN STUDYING IMMUNE RESPONSES TO TUBERCULOSIS

Dr Joanna Kirman's Infectious Diseases research team is part of an international effort focused on reducing the incidence of tuberculosis (TB) through the development and implementation of more effective TB vaccines.

"Our struggle to develop a good TB vaccine has stemmed in part from a poor understanding of the immune mechanisms that orchestrate protection against TB," says Dr Kirman.

Protective immunity to TB is dependent on $CD4^+$ T cells. To determine which specific subset of $CD4^+$ T cells mediate protection against TB, many researchers have used adoptive transfer of T cells from immunised or infected mice into immune-deficient recipient mice. They then challenge the mice with TB to determine whether the T cells can protect against the infection.

"In collaborative work with Prof Brett Delahunt from the University of Otago, Wellington, which has just been published in the journal *Tuberculosis*, we showed that this model has a major flaw," says Dr Kirman. "Our research showed that transfer of some T cell subsets causes colitis and systemic T cell activation in the recipient mice. This may influence the outcome of a challenge infection and enhance protection in a non-specific way, which would not occur in an intact mouse."

This study raises important doubts about the validity of using the popular adoptive transfer model to study $CD4^+$ T cell mediated protection against TB. The development of an improved model is currently underway.

Ancelet L, Rich FJ, Delahunt B, Kirman JR Dissecting memory T cell responses to TB: Concerns using adoptive transfer into immunodeficient mice. Tuberculosis (Edinb), (in press)

RESEARCH HIGHLIGHT

DR TIFFANY BOUCHERY-SMITH JOINS OUR PARASITOLOGY RESEARCH TEAM

Human hookworm infection is currently controlled through frequent use of antihelminthic drugs in school-age children, however high rates of re-infection occur soon after treatment and there is evidence of emerging drug resistance.

Vaccination is currently viewed as the only long-term solution for reducing the enormous burden this disease imposes on developing countries. Before we can start developing a vaccine against the parasite however, we first need to identify the immune mechanisms that can best protect against hookworm infection.

These research endeavours have been greatly strengthened by French immunoparasitologist Dr Tiffany Bouchery-Smith joining our research team. Dr Bouchery-Smith recently completely her doctoral research on the role of chemokines in the survival, development and reproduction

Dr Tiffany Bouchery-Smith.

of *Litomosoides sigmodontis* (a filarial parasite) in the Comparative Parasitology Group of the Museum National d'Histoire Naturelle (National Museum of Natural History) in Paris.

With the support of a Malaghan Institute Postdoctoral Fellowship, Dr Bouchery-Smith will investigate the early stages of infection of *Nippostrongylus brasiliensis*, a rodent model of human hookworm infection, to understand the natural entrance of the parasite, its migration pathway from the skin to the lungs, and how this pathway can be affected by a protective immune response.

Multiple Sclerosis

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system that results in functional disability and can render a person unable to write, speak or walk. Women are almost three times more likely to develop MS than men. While some MS treatments are available to help manage the disease, they are not equally effective in all patients and often have side effects associated with medium to long-term use.

Researchers at the Malaghan Institute are using a multipronged approach to develop more effective therapies for controlling the aberrant immune responses that occur in organ specific autoimmune disorders such as MS.

The first approach is to understand the basic biology of MS in experimental laboratory models, in order to identify potential therapeutic targets or new markers of disease progression. In conjunction with this work is a research programme aimed at identifying and testing novel agents that could be used to halt disease progression. One compound, MIS416, is produced by the New Zealand Company Innate Immunotherapeutics and has just completed a Phase 2A clinical trial in secondary progressive MS patients.

Research Associate Dr Anne La Flamme, who is an Associate Professor in the School of Biological Sciences at Victoria University of Wellington, is responsible for overseeing the Malaghan Institute's MS research. Malaghan Institute Research Group Leader Dr Jacquie Harper has also undertaken autoimmunity research as part of her greater Arthritis and Inflammation research programme.

Multiple sclerosis affects one in every 1,500 New Zealanders – one of the highest frequencies of this disease worldwide.

Kitty Johnson (centre) from the Great NZ Trek presenting their cheque to MS group PhD students.

RESEARCH HIGHLIGHT

HOW SUPPORT FROM THE GREAT NEW ZEALAND TREK IS HELPING PROGRESS OUR MS RESEARCH

Since 2010, funds from the Great New Zealand Trek Charitable Trust have supported several of our MS research projects. These projects have focused on identifying new treatments for MS as well as on understanding how immune responses are altered during the disease.

"Overall, funds from the Great New Zealand Trek have been vital in allowing us to investigate and test new ideas, while also supporting the development of emerging MS researchers," says Dr Anne La Flamme.

One project, in particular, focuses on how monocyte activation is altered during MS. Monocytes are a type of immune cell found in the blood, and recent work has shown that glatiramer acetate (GA), also known as Copaxone, alters the activation state of these cells.

"In work funded by the Great New Zealand Trek, we have been studying how GA alters monocyte activation and compared this state to that induced by intravenous gammaglobulin (intravenous antibody), which has also been used to treat MS but with limited success," says Dr La Flamme. "In particular, we would like to determine if we can predict if an MS patient will respond to GA by the effects of this drug on their monocyte responses."

These studies are being conducted by PhD student Delgertsetseg Chuluundorj, in collaboration with Drs Scott Harding and David Abernathy from Wellington Hospital.

"We thank all of the MS patients who have graciously donated their blood for this research - this study would not be possible without their support."

RESEARCH HIGHLIGHT

INNATE IMMUNOTHERAPEUTICS

MIS416 is a novel microparticle derived from *Propionibacterium acnes* comprising a minimal cell wall skeleton rich in immunostimulatory muramyl dipeptide (MDP) and bacterial single stranded DNA, which signal through the innate immune receptors, NOD2 and TLR9, respectively.

While originally developed as a vaccine adjuvant, interest has grown around the potential use of MIS416 as a standalone immunomodulatory agent for the treatment of inflammatory disorders when administered systemically.

"Based on positive anecdotal findings from a compassionate-use program in secondary progressive MS patients, a formal Phase 2A trial has just been completed to evaluate the safety, tolerability and initial impact of MIS416 in progressive MS," says Dr La Flamme. "The results from this trial have met or exceeded expectations and a larger-longer Phase 2B trial in patients with SPMS is planned to commence in 2013."

"In parallel at the Malaghan Institute, we are investigating MIS416's mechanism of protection using the mouse model of MS, experimental autoimmune encephalomyelitis (EAE)."

"Previously, we found that MIS416 significantly reduced neurological disease when administered before or after the onset of neurological symptoms in both progressive and relapsing-remitting models of MS," says Dr La Flamme.

"Furthermore, we found that MIS416 modulated the systemic immune response to dampen down inflammatory responses, and preliminary results show that these alternations in turn reduced CNS inflammation."

These findings have just been submitted for publication.

RESEARCH HIGHLIGHT

DISSECTING THE MECHANISMS OF ACTION OF THE MS DRUG GLATIRAMER ACETATE

Glatiramer acetate (GA) is an immunomodulator drug approved by the Food and Drug Administration (FDA) for treating relapsing-remitting multiple sclerosis (MS). Although previous studies have shown that GA relieves clinical symptoms in patients with MS and suppresses experimental autoimmune encephalomyelitis (EAE – an animal model of MS) in mice, its mechanism of action is not yet fully understood.

To expand our understanding of the suppressive mechanisms of GA, and elucidate whether GA targets specific subsets of immune cells, Masters student Aras Toker investigated the association between GA treatment and blood monocyte function. Monocytes are a type of white blood cell that moves quickly to sites of infection to stimulate inflammatory responses. They are also capable of suppressing inflammation in certain disease contexts.

"Aras' research showed that GA enhances the ability of blood monocytes to suppress the inappropriate inflammatory responses of the T cells that damage the central nervous system," says Dr Jacquie Harper. "Our findings identify additional mechanisms involved in GA-dependent suppression of autoimmune reactivity and illustrate that the different routes of GA administration could be used to engage multiple immunosuppressive pathways in the treatment of MS."

This study highlights the potential for utilising alternative routes for GA administration to enhance its therapeutic efficacy. Dr Harper says they will also look to expand their understanding of the immunosuppressive effects of the monocytes identified in this research, to determine if they can be specifically targeted to develop a therapy for treating MS and other autoimmune conditions.

Toker A, Slaney CY, Bäckström BT, Harper JL (2011) Glatiramer acetate treatment directly targets CD11b+Ly6G- monocytes and enhances the suppression of autoreactive T cells in experimental autoimmune encephalomyelitis. Scand J Immunol, 74:235-43

Other Areas of Research & Development

RESEARCH HIGHLIGHT

FINDING A WAY TO PROMOTE CELL SURVIVAL IN INDIVIDUALS WITH MOTOR NEURONE DISEASE

In a research programme supported by the Estates of Ellen, Sinclair, Barbara and Alison Wallace, Dr Melanie McConnell and Masters student Susanna Brow are using their knowledge of cell survival to identify ways to prolong the life of neurons in individuals with motor neurone disease (MND).

Susanna Brow.

Patients with MND suffer increasing weakness of the muscles, due to the death of the neurons that feed into them and there is currently very little that can be done to prevent this. Dr McConnell and Susanna believe that targeting the activity of the cell survival protein SIRT1 might hold the key to delaying or preventing neurodegeneration.

SIRT1 is a key mediator of stress responses and has been shown to be upregulated in neurons. However, little is known about its expression in neighbouring astrocytes, which play a critical role in signalling to neurons to keep them alive. Dr McConnell and Susanna are addressing this question by treating normal astrocyte cells with stresses that induce a MND phenotype, before and after SIRT1 activation. Careful examination of the precise effects of SIRT1 activation in these cells will aid in the development of approaches for treating individuals with motor neurone disease.

"This year we were fortunate to have our collaborator Dr Mahmoud Kiaei visit us from the University of Arkansas for Medical Sciences," says Dr McConnell. "Dr Kiaei uses transgenic mouse models of the neurological disorder ALS [amyotrophic lateral sclerosis], as well as primary astrocytes and motor neurons, to study the pathogenesis of motor neuron degeneration. Having the benefit of Dr Kiaei's expertise was therefore invaluable for our own research."

"We also look forward to utilising our knowledge and experience in this area in collaborative research with scientists from Massey University." M

RESEARCH HIGHLIGHT

LYMPHANGIOLEIOMYOMATOSIS (LAM)

Dr James Baty.

Lymphangioleiomyomatosis (LAM) is a progressive and invariably fatal rare lung disease that afflicts young women in their reproductive years. It causes shortness of breath, chest pains, coughing and lung collapse and there is no known cure.

While LAM is not presently classified as a cancer, LAM cells have cancer cell-like properties including loss of cell growth control and abnormal differentiation, and there is evidence for LAM cell metastasis from lung tissue.

Since November 2009 the New Zealand LAM Trust/LAM Australasia Research Alliance has helped fund research by Dr James Baty and Prof Mike Berridge to explore the feasibility of treating LAM using the immunological therapies being developed for treating cancer.

"By working closely with New Zealand LAM Trust Director, Bronwyn Gray," says Dr Baty "we hope that one day we can help ease the suffering of individuals affected by this devastating disease."

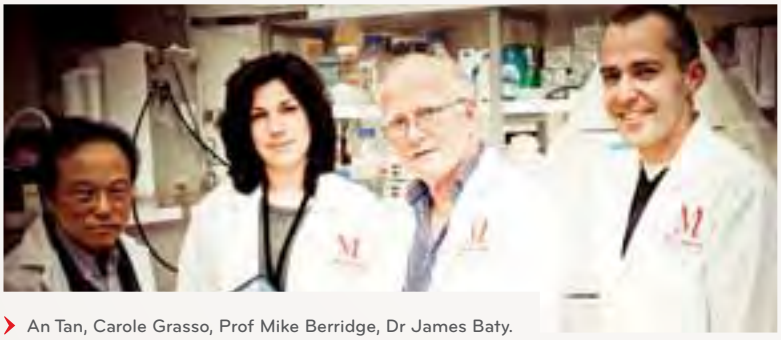
RESEARCH HIGHLIGHT

MOBILITY OF MITOCHONDRIA BETWEEN MAMMALIAN CELLS

Most energy production in complex organisms occurs in mitochondria. These cellular organelles originated over three billion years ago in a symbiotic event involving two bacteria, one of which engulfed another that burned oxygen to generate energy.

Today, mammalian mitochondria have retained a small residual genome that encodes essential components of the respiratory chain and bacteria-like protein synthetic machinery. With few exceptions, mitochondria are retained within their cell of origin. Without mitochondria, development, movement and brain function would be impossible.

Working with melanoma and breast cancer cells purged of their mitochondrial genome, An Tan and Prof Mike Berridge have shown quite unexpectedly that these cells fail to form tumours in mice until a replacement genome is acquired. Together with Dr James Baty, they have shown unequivocally that this replacement genome came from normal cells in the local microenvironment.



An Tan, Carole Grasso, Prof Mike Berridge, Dr James Baty.

"We have shown for the first time that the mitochondrial genome is mobile and can move horizontally between cells under physiological conditions," says Prof Berridge. "As previous cell culture experiments have shown that mitochondria can move between cells through membrane nanotubes, this is the most likely explanation for our results."

Do tumour cells and other cells in the body that sustain mitochondrial genome damage, for example in muscular and neurological diseases, in a group of diseases called the mitochondriopathies, and in ageing and tissue repair use mitochondrial replacement to correct this damage?

"Future research will address these questions," says Prof Berridge. "By developing novel mitochondrial genome markers and using them to track mitochondrial genome movement between cells in health and in disease."

Immunoglycomics

Underpinning our cancer, tuberculosis and asthma research programmes is a rapidly growing field of innovation termed immunoglycomics. Immunoglycomics is the study of how carbohydrates, either linked to other chemical species (glycoconjugates) or as individual compounds (for example 'carbohydrate mimics'), can be used to influence immune responses.

A classic example of an immune-stimulating glycolipid isolated from a marine sponge is α-galactosylceramide (α-GalCer), which has been shown to boost the immune response in favour of enhanced anti-tumour activity. While the tumour-derived peptide effectively acts as the 'ignition' and turns the immune response on, the glycolipid acts as the 'throttle' and controls the intensity of the immune response.

Bacteria contain many complex carbohydrates in their cell walls that have immunomodulatory properties. Understanding how these bacterial components are able to influence the host immune response is another area of immunoglycomics research being undertaken at the Malaghan Institute. This, in turn, will lead to the development of better therapeutics and vaccination strategies, not only for infectious diseases such as tuberculosis, but also for the treatment of cancer and allergy.

Carbohydrate mimics can also be used to control the way in which more complex carbohydrates (chains of carbohydrates) are synthesised or degraded. This has application in a number of diseases, including bacterial infection, diabetes and lysosomal storage disorders. For example, azasugar carbohydrate mimics have been used by our Immunoglycomics team, led by Dr Bridget Stocker, as a starting point for the development of anti-TB drugs and also for drugs against Gaucher's disease.

RESEARCH HIGHLIGHT

GOING TO ANY LENGTH?

While the therapeutic activity of bacterial cell wall extracts has long been recognised, what isn't well understood is what specific components of the cell wall are responsible for influencing the immune response.

To tease apart the exact immunomodulatory potential of specific cell wall components, PhD student Ashna Khan and Research Officer Stephanie Chee, both members of Dr Bridget Stocker's Immunoglycomics Research Group, synthesised a variety of glycolipids called trehalose dimycolates (TDMs). TDMs are a class of compounds found in the cell walls of mycobacteria such as tuberculosis (TB). The group then investigated how the length of these lipids influenced the innate immune response by measuring macrophage activation.

"We were the first to show that there is a correlation between trehalose diester lipid length and macrophage activation," says Dr Stocker. "Longer lipids stimulated macrophage activation more effectively than shorter lipids."

Ashna Khan.

This work, which featured on the cover of the *ChemBioChem* journal at the end of 2011 due to its high scientific merit, is important in understanding the pathogenicity of TB. It may also have future application in the development of adjuvants for TB and other diseases.

Khan AA, Chee SH, McLaughlin RJ, Harper JL, Kamena F, Timmer MS, Stocker BL (2011) Long-chain lipids are required for the innate immune recognition of trehalose diesters by macrophages. ChemBioChem, 12:2572-6 [Also featured on journal cover]

Alfonso Schmidt, Kylie Price.

Cell Technology Suite

The Cell Technology Suite now encompasses the most important technological platforms available to researchers at the Malaghan Institute, which are flow cytometry, immunohistochemistry and microscopy.

By far the most highly utilised and powerful research tool of those mentioned is flow cytometry. This technique allows scientists and clinicians to understand cells based on the fingerprint of the markers they express. The applications of flow cytometry are immense. For instance, it is now recognised that when a cancer-killing immune cell invades a tumour, the tumour produces chemicals that slow down its activity. Flow cytometry enables the scientist to purify this immune cell and to determine what type of stimulus is needed to reinstate its cancer-killing function.

Our Cell Technology team, led by Hugh Green Flow Cytometry Fellow Kylie Price, provides expert training and advice on using these technologies, from sectioning on the cryostat (a micron-thin tissue slicer that cuts frozen samples), to staining sections for immunohistochemical analysis, and lastly to visualising them under the fluorescence microscope. The Cell Technology Suite is intended to be the one-stop shop for the analysis, purification and characterisation of cells.

The Cell Technology Suite also provides the same services to the wider scientific community. In addition to supporting health research focused groups in Auckland and Otago the team work with Fertility Associates and several departments at Victoria University of Wellington. Their goal is to encourage interested scientists to utilise these techniques to advance discoveries within their own fields of research.

To keep on top of this rapidly evolving field, Kylie is currently overseas undertaking a technology transfer sabbatical. The new knowledge Kylie is gaining in the capabilities and applications of multicolour flow cytometry will be invaluable for all our research programmes.

RESEARCH HIGHLIGHT

EXTENSION OF OUR MULTICOLOUR FLOW CYTOMETRY PLATFORM

With the support of the New Zealand Lottery Grants Board (Health Research) and The Thompson Family Foundation Inc, the Malaghan Institute purchased a new flow cytometer this year called the LSR Fortessa by Becton Dickinson. This is our second multicolour cytometer, capable of studying numerous cell characteristics at a single pass.

This investment reinforces our position as New Zealand's leading flow cytometry facility. Acquiring the Fortessa means the Cell Technology Suite is now better positioned to support the melanoma cancer vaccine trial that will begin next year. These multicolour cytometers are crucial for maximising the information recovered from each precious patient sample. It is our aim to develop strong immunophenotyping capabilities during all the phases of this clinical trial, which will have positive consequences for every research group at the Malaghan Institute.

Brigitta Mester.

THE CELL TECHNOLOGY TEAM

Manager:
Kylie Price BSc(Otago), MSc(Hons)(VUW)

Research Assistants:
Brigitta Mester MSc(Hungary),
Alfonso Schmidt BSc(Chile)

Research Funding

AgResearch Ltd, Hamilton

To Prof Le Gros to support the project *Immunomodulation of the inflammatory responses that result from adverse reactions to milk.*

Arthritis New Zealand

To Dr Harper to support the project *Impact of hyperuricaemia on monocyte/macrophage phenotype in gouty arthritis.*

BEA Trust

Towards the purchase of a Gel Logic Imaging System.

Cancer Society of New Zealand (National Body)

To Prof Berridge to support the project *Intercellular mitochondrial transfer in tumorigenesis and metastasis.*

To Assoc Prof Hermans and Prof Berridge to support the project *Targeting tumour stem cells to improve immunotherapy.*

To Assoc Prof Hermans and Mr Hunn to support the project *Using dendritic cell immunisation to sensitise malignant glioma to chemotherapy.*

To Dr McConnell and Assoc Prof Hermans to support the project *How does chemotherapy alter the immunophenotye of glioblastoma multiforme?*

To Dr McConnell and Mr Hunn to support the project *Does BCL6 drive chemotherapy resistance in glioblastoma multiforme?*

To Dr Stocker to support the project *Glycolipid adjuvants: enhancing cancer vaccines.*

To Taryn Osmond and Assoc Prof Hermans to support the PhD project *Mechanisms of induction of anti-tumour responses by dendritic cells.*

Cancer Society of New Zealand (Wellington Division)

To Prof Berridge and Dr Baty to support the project *Tracking intercellular mitochondrial movement in tumorigenesis and metastasis.*

To Dr Petersen to support the project *Developing prime-boost strategies for α-GalCer-containing cancer vaccines.*

To Dr Stocker to support the project *Phytosphingosine functionalised glycolipids as adjuvants to understand the effects of the carbohydrate head group in cancer immunotherapy.*

Child Health Research Foundation

To Prof Berridge to support the project *Activating the immune system against cancer: application of dendritic cell immunotherapy to childhood brain cancers and central nervous system leukaemia.*

Frank Millar & Co Wellington Ltd, Industrial & Commercial Electricians

To support the operational costs of the flow cytometry laboratory within the Cell Technology Suite.

Fonterra Co-operative Group Ltd

To Dr Forbes-Blom and Prof Le Gros to support the project *Tolerogenic effects of milk protein hydrolysates.*

Foundation for Research, Science & Technology

Post-doctoral Fellowship awarded to Dr Forbes-Blom to support the project *Getting to the guts of allergic inflammation.*

To Dr Harper to support the projects *Berry fruits for treating inflammation* and *Fruit foods for inappropriate inflammation.*

To Assoc Prof Hermans and Dr Harper to support the project *Carbohydrate nanotechnology – large, carbohydrate containing immunopharmaceuticals.*

To Prof Le Gros to support the project *Anti-allergy ingredients from raw milk.*

To Prof Ronchese to support the project *Reversing evolution – making lambs immune to worms.*

Genesis Oncology Trust

To Prof Berridge to support the project *Combining immunotherapy with targeted drug therapy in melanoma: effects of the $BRAF^{V600E}$-targeting drug, PLX4720 on anti-tumour immune responses.*

To Dr McConnell to support the project *BCL6 and chemoresistance: a new target for glioblastoma multiforme therapy?*

To Dr Stocker to support the project *TDMs as potent immunomodulators in cancer therapy.*

Health Research Council of New Zealand

To Dr Ferguson to support a clinical fellowship for the project *Novel magnetic nanoparticles as contrast agents for magnetic resonance imaging* and Mr Hunn to support a clinical fellowship for the project *Improving immunotherapy for high grade glioma.*

To Dr Forbes-Blom and Prof Le Gros to support the projects *New strategies for the treatment and prevention of food allergy* and *Cellular mechanisms underlying food allergen sensitisation.*

To Dr Harper (originally to Assoc Prof Bäckström) to support the project *Inhibition of autoimmune diseases by superantigen-peptide conjugates.*

To Assoc Prof Hermans to support the programme *Vaccine-based immunotherapy of cancer.*

To Assoc Prof Hermans and Dr Petersen to support the project *Mechanisms of induction of anti-tumour immune responses by dendritic cells.*

To Dr Kirman to support the project *Whiti Te Ra: bronchiolitis disparities among Maori and Pacific children.*

To Prof Le Gros to support the projects *Candidate cytokines involved in allergic airway disease* and *Novel vaccine approaches for protecting against helminth parasites.*

To Prof Ronchese, Dr Forbes-Blom and Prof Le Gros to support the project *Immunotherapy of allergic disease.*

To Prof Ronchese and Prof Le Gros to support the projects *Role of dendritic cells in allergic sensitisation* and *Cytotoxic T lymphocyte-mediated immunotherapy of allergic airway inflammation.*

To Prof Ronchese, Dr Peng and Dr Jordan to support the project *Defining the characteristics of effective anti-tumour T cells.*

To Dianne Sika-Paotonu and Assoc Prof Hermans to support the project *Increasing the potency of dendritic cell-based vaccines for the treatment of cancer.*

To Dr Stocker and Prof Le Gros to support the project *Deciphering the molecular fingerprint of allergens.*

To Dr Stocker, Dr Timmer and Prof Ronchese to support the project *Glycolipids in anti-cancer vaccines.*

Hugh Green Foundation

To support the flow cytometry laboratories within the Cell Technology Suite and Kylie Price as the Hugh Green Fellow.

Industrial Research Limited

To Dr Forbes-Blom and Prof Le Gros to support the project *Development of GL-2, isolated from Bifidobacteria infantis.*

To Assoc Prof Hermans to support the *DC vaccine adjuvant* project.

Just Paterson Real Estate (in memory of Sally Paterson)

To Assoc Prof Hermans to support glioblastoma research.

Keith Seagar Research Fund

To support cancer research.

Maurice Wilkins Centre for Molecular Biodiscovery

To Dr Kirman to support the project *Development and testing of novel DNA and protein 'dormancy' vaccines against Mycobacterium tuberculosis.*

To Dr McConnell to support the project *Does P13K signalling maintain the stem-like phenotype of brain cancer cells?*

Melanoma Research Alliance

To Prof Berridge and Dr McConnell to support the project *Therapeutic targeting of melanoma stem cells.*

New Zealand LAM Trust/LAM Australasia Research Alliance

To Prof Berridge and Dr Baty to support the project *Self-renewal properties of LAM cells.*

New Zealand Lottery Grants Board - Health Research

To Dr Harper to support the project *MSU, inflammation, monocyte differentiation, M-CSF, GM-CSF, gout.*

To Dr Kirman to support the project *Identifying memory $CD4^+$ T cell subsets that protect against Tuberculosis.*

Equipment grant awarded to Kylie Price and Prof Le Gros towards purchase of Becton Dickinson LSR Fortessa flow cytometer.

To Prof Ronchese to support the project *Activation of intra-tumoural dendritic cells for anti-tumour immunity.*

To Dr Stocker to support the projects *TDMs as vaccine adjuvants for the prevention of M. tuberculosis* and *Alkenylamine inhibitors of M. tuberculosis.*

To Dr Stocker and Prof Le Gros to support the project *A sweet solution to asthma.*

Rex & Betty Coker Foundation

To Prof Le Gros to support a PhD scholarship.

Rotary Club of Port Nicholson

To support the operating costs of the Immunohistochemistry Station.

Rotary Club of Wellington

A scholarship to Naomi Baker to support the PhD project *Th2 immune responses in vivo.*

Springhill Charitable Trust and Frimley Foundation

To Dr Forbes-Blom to support the project *Histopathologic findings in experimental food allergy.*

The Dr Marjorie Barclay Trust

To Prof Le Gros to support asthma research.

The Estate of Alan McLean Duncan

To support cancer research.

The Estate of PM Matthews

Towards the purchase of two refrigerated benchtop centrifuges.

The Estate of WJ Thomson

To Dr Harper to support the project *Mechanism of UA-induced effects on inflammation.*

The Estate of Isabel Mary Tucker

To support brain cancer research.

The Estates of Ellen, Sinclair, Barbara and Alison Wallace

To Dr McConnell to support the project *Sirt 1 protein.*

To Dr McConnell to support the Stem Cell research programme and Immunohistochemistry Station.

The Graham Hall Bequest

To Mr Hunn to support the project *Dendritic cell therapy for high grade glioma.*

The Great New Zealand Trek Charitable Trust

To Dr La Flamme to support multiple sclerosis research.

The Neurological Foundation of New Zealand

To Dr La Flamme to support multiple sclerosis research.

The Royal Society of New Zealand Marsden Fund

To Assoc Prof Hermans and Dr Petersen to support the project *Towards better vaccines: investigating the role of langerin^{+} CD8α^{+} dendritic cells in innate and adaptive immunity.*

To Dr Stocker to support the project *Mincle – the secret weapon in the development of trojan liposomes to target dysfunctional macrophages.*

The Thompson Family Foundation, Inc. through the Victoria University of Wellington Foundation

To support the cancer vaccine programme.

University of Otago

To Dr Herst and Dr McConnell to support the project *The effect of high dose ascorbate on radiosensitisation of glioblastoma and normal cells.*

To support the research of visiting PhD student Sara McKee.

Wade Thompson

To support the cancer vaccine programme.

Wellington Medical Research Foundation

To Prof Berridge and Dr Baty to support the project *Self-renewal properties of LAM cells.*

To Dr Harper to support the projects *Impact of urate-lowering therapy on monocyte/macrophage phenotype in gouty arthritis, The role of CSFs and TGF-β in pro-inflammatory macrophage differentiation* and *The impact of obesity and hyperuricemia on inflammatory immune regulation.*

To Dr Joanna Kirman to support the project *Characterising protective CD4^{+} memory T cell subsets that mediate protection against Tuberculosis.*

To Dr McConnell to support the project *Immune targeting of glioblastoma multiforme – can NK cells kill chemo-resistant cancers?*

To Dr Petersen to support the project *Painting cancer cells with immuno-modulatory antibodies: a novel approach to improve cancer vaccines.*

To Prof Ronchese to support the project *Activation of intra-tumoral dendritic cells for anti-tumour immunity.*

To Dr Stocker to support the project *Fluorescent probes to study glycolipid uptake and trafficking in cancer immunotherapy.*

Education

The success of the Malaghan Institute is dependent on the calibre of the people who do their research here. For this reason, we have always had an active commitment to education. We wish to foster the development of new scientists and to expose students to the most recent advances in immunology and related topics.

The Malaghan Institute has a long-standing affiliation with New Zealand universities and is held in high regard as one of the foremost organisations for students to complete a Doctorate of Philosophy (PhD) in immunology. Students who undertake postgraduate research here are sought after around the world because of the extensive training they receive.

We currently have 24 postgraduate students enrolled in PhD, Masters and Honours research programmes. Each summer we also host undergraduate students who have an interest in science and are of the calibre to take on and benefit from an assigned research project. Working with close direction from the Institute's Research Group Leaders and senior research staff, the students are able to conduct meaningful work and learn what a career in research offers.

We are proud of our reputation for mentoring New Zealand's brightest and most creative postgraduate students.

Lindsay Ancelet.

STUDENT HIGHLIGHT

INFECTIOUS BY DISEASE, INFECTIOUS BY NATURE

Freely admitting to being someone that "wears her heart on her sleeve," PhD student Lindsay Ancelet's love of research is as infectious as the *Mycobacterium tuberculosis* bacteria she studies.

The overall goal of Lindsay's PhD research is to create a better vaccine for tuberculosis (TB), by understanding how the immune system responds to the bacteria that cause the disease. Under the supervision of Dr Joanna Kirman, Lindsay has successfully navigated her way through the many challenges that come with working with such a lethal microorganism.

All the long hours have been worth it however, with the success of Lindsay's research culminating in three scientific publications, an invitation to present her research at an international tuberculosis conference earlier this year, and the potential application of her collaborative TB vaccine work in a human clinical study. Not bad for a self-confessed "science geek" from small town Canada.

Lindsay says that she knew from a young age that she would do a PhD in science. "I have always felt passionate about science," she says. "I love the idea of contributing new knowledge to the world, especially knowledge that could lead to an improved therapy for disease."

While tuberculosis is the current focus of her research, Lindsay started out in breast cancer, completing a Masters degree at the University of Toronto. She came to New Zealand in 2009 to learn more about how our body responds to something foreign, whether it is cancer or infectious organisms, and looks forward to building on this knowledge in her future career.

Lindsay is a shining example of what it takes to be a great scientist – curiosity, intelligence and commitment, and we wish her every success for the future.

Publications

2011

Ainge GD, Martin WJ, Compton BJ, Hayman CM, Larsen DS, Yoon SI, Wilson IA, Harper JL, Painter GF (2011) Synthesis and Toll-like receptor 4 (TLR4) activity of phosphatidylinositol dimannoside analogues. **J Med Chem,** 54:7268-79

Chan ST, Pearce AN, Januario AH, Page MJ, Kaiser M, McLaughlin RJ, Harper JL, Webb VL, Barker D, Copp BR (2011) Anti-inflammatory and anti-malarial meroterpenoids from the New Zealand ascidian *Aplidium scabellum*. **J Org Chem,** 76:9151-6

Khan AA, Chee SH, McLaughlin RJ, Harper JL, Kamena F, Timmer MS, Stocker BL (2011) Long-chain lipids are required for the innate immune recognition of trehalose diesters by macrophages. **ChemBioChem,** 12:2572-6 [Also featured on cover]

Shaw OM, Harper JL (2011) Bradykinin receptor 2 extends inflammatory cell recruitment in a model of acute gouty arthritis. **Biochem Biophys Res Commun,** 416:266-9

Toker A, Slaney CY, Bäckström BT, Harper JL (2011) Glatiramer acetate treatment directly targets CD11b+Ly6G- monocytes and enhances the suppression of autoreactive T cells in experimental autoimmune encephalomyelitis. **Scand J Immunol,** 74:235-43

Win-Mason AL, Jongkees SA, Withers SG, Tyler PC, Timmer MS, Stocker BL (2011) Stereoselective total synthesis of aminoiminohexitols via carbamate annulation. **J Org Chem,** 76:9611-21

2012

Ancelet L, Kirman J (2012) Shaping the $CD4^+$ memory immune response against tuberculosis: the role of antigen persistence, location and multi-functionality. **BioMol Concepts,** 3:13-20

Ancelet L, Rich FJ, Delahunt B, Kirman JR Dissecting memory T cell responses to TB: Concerns using adoptive transfer into immunodeficient mice. **Tuberculosis (Edinb),** (in press)

Cheong S, Ferguson P, Hermans IF, Jameson GN, Prabakar S, Herman DA, Tilley RD (2012) Synthesis and stability of highly crystalline and stable iron/iron oxide core/shell nanoparticles for biomedical applications. **ChemPlusChem,** 77:135-40

Dangerfield EM, Cheng JM, Knight DA, Weinkove R, Dunbar PR, Hermans IF, Timmer MS, Stocker BL (2012) Species-specific activity of glycolipid ligands for invariant NKT cells. **ChemBioChem,** 13:1349-56

Dangerfield EM, Gulab SA, Stocker BL, Timmer MS The synthesis of carbamates from alkenylamines. **Carbohydrate Chemistry: Proven Methods,** Volume II (in press)

Dangerfield EM, Wu Z, Tyler PC, Timmer MS, Stocker BL Reductive amination methodology for the protecting-group-free synthesis of primary amines. **Carbohydrate Chemistry: Proven Methods,** Volume II (in press)

Enomoto N, Hyde E, Ma JZ, Yang J, Forbes-Blom E, Delahunt B, Le Gros G, Ronchese F (2012) Allergen-specific CTL require perforin expression to suppress allergic airway inflammation. **J Immunol**, 188:1734-41

Forbes-Blom E, Camberis M, Prout M, Tang SC, Le Gros G (2012) Staphylococcal-derived superantigen enhances peanut induced Th2 responses in the skin. **Clin Exp Allergy,** 42:305-14

Herst PM, Berridge MV Cell hierarchy, metabolic flexibility and systems approaches to cancer treatment. **Curr Pharm Biotechnol,** (in press)

Herst PM, Broadley KW, Harper JL, McConnell MJ (2012) Pharmacological concentrations of ascorbate radiosensitize glioblastoma multiforme primary cells by increasing oxidative DNA damage and inhibiting G2/M arrest. **Free Radic Biol Med,** 52:1486-93

Khan AA, Chee SH, Stocker BL, Timmer MS (2012) The synthesis of long-chain α-alkyl-β-hydroxy esters using allylic halides in a Fráter-Seebach alkylation. **Eur J Org Chem,** 2012:995-1002

Khan AA, Stocker BL, Timmer MS (2012) Trehalose glycolipids-synthesis and biological activities. **Carbohydr Res,** 356:25-36

Klionsky DJ et al (2012) Guidelines for the use and interpretation of assays for monitoring autophagy. **Autophagy**, 8:445-545

Leong AG, Herst PM, Harper JL (2012) Indigenous New Zealand honeys exhibit multiple anti-inflammatory activities. **Innate Immun,** 18:459-66

Lim S N, Kuhn S, Hyde E, Ronchese F Combined TLR stimulation with Pam3Cys and Poly I:C enhances Flt3-ligand dendritic cell activation for tumor immunotherapy. **J Immunotherapy,** (in press)

Liu X, Chia E, Shaw OM, Martin WJ, Harper JL Rapid CCL2 release by membrane stromal cells initiates MSU crystal-induced monocyte recruitment in a peritoneal model of gouty inflammation. **Eur J Inflamm,** (in press)

Ma JZ, Lim SN, Qin JS, Yang J, Enomoto N, Ruedl C, Ronchese F (2012) Murine $CD4^+$ T cell responses are inhibited by cytotoxic T cell-mediated killing of dendritic cells and are restored by antigen transfer. **PLoS One,** 7:e37481

Matilainen H, Yu XW, Tang CW, Berridge MV, McConnell MJ (2012) Sphere formation reverses the metastatic and cancer stem cell phenotype of the murine mammary tumour 4T1, independently of the putative cancer stem cell marker Sca-1. **Cancer Lett,** 323:20-8

McKee SJ, Young VL, Clow F, Hayman CM, Baird MA, Hermans IF, Young SL, Ward VK (2012) Virus-like particles and α-galactosylceramide form a self-adjuvanting composite particle that elicits anti-tumour responses. **J Control Release,** 159:338-45

Meyer KJ, Singh AJ, Cameron A, Tan AS, Leahy DC, O'Sullivan D, Joshi P, La Flamme AC, Northcote PT, Berridge MV, Miller JH (2012) Mitochondrial genome-knockout cells demonstrate a dual mechanism of action for the electron transport complex I inhibitor mycothiazole. **Mar Drugs,** 10:900-17

Min B, Brown MA, Le Gros G (2012) Understanding the roles of basophils: breaking dawn. **Immunology,** 135:192-7

Rich FJ, Kuhn S, Hyde EJ, Harper JL, Ronchese F, Kirman JR Induction of T cell responses and recruitment of an inflammatory dendritic cell subset following tumour immunotherapy with *Mycobacterium smegmatis*. **Cancer Immunol Immunother,** (in press)

Robinson M, McConnell MJ, Le Gros G How epigenetic imprinting contributes to stabilizing the Th2 phenotype. **Immunol Cell Biol,** (in press)

Salinas I, Anderson SA, Wright J, Webb VL (2012) *In vivo* innate immune responses of groper (*Polyprion oxygeneios*) against *Miamiensis avidus* infection and lack of protection following dietary vitamin C administration. **Fish, Shellfish Immunol,** 32:8-15

Sauvageau J, Foster AJ, Khan AA, Chee SH, Sims IM, Timmer MSM, Stocker BL Synthesis and biological activity of the LTA glycolipid anchor from *Streptococcus sp. DSM 8747*. **ChemBioChem,** (in press)

Sauvageau J, Ryan J, Lagutin K, Sims IM, Stocker BL, Timmer MS (2012) Isolation and structural characterisation of the major glycolipids from *Lactobacillus plantarum*. **Carbohydr Res,** 357:151-6

Stocker BL, Win-Mason AL, Timmer MS (2012) I_2-mediated carbamate annulation: scope and application in the synthesis of azasugars. **Carbohydr Res,** 356:163-71

Full details of all 'in press' publications will appear in the 2012/2013 Annual Report.

Seminars

Scientific knowledge gained through research in the laboratory is of little value unless it is shared with the greater scientific community. For the most part this is achieved through publications in scientific journals, however these are often not accessible until many months or even years after the original research was undertaken. This is why oral presentations or seminars are so valuable.

Seminars provide a forum for sharing latest research developments, while also encouraging open debate and discussion with the scientists involved. This year we have been fortunate to enjoy many high calibre presentations at the Malaghan Institute, the details of which are listed on the following two pages.

Our senior research staff were also invited to present their work at prestigious research institutes and international conferences across the globe including Australia, Canada, Norway, England, Greece, Ireland, Italy, Peru, Singapore, Spain, and the United States of America. This knowledge sharing is vital for us to make our mark on the world, while also establishing meaningful collaborations with scientists that share common research goals.

Prof Manfred Kopf.

2011

August

Dr Irene Salinas, Malaghan Institute. Understanding the integration of mucosal immune responses: what can we learn from teleost fish?

Dr Simon Phipps, University of Queensland, Brisbane, Australia. Defective toll-like receptor 7 signalling underlies the inception and exacerbations of asthma

Dr Jacquie Harper, Malaghan Institute. Monocyte trafficking, differentiation and inflammatory function in gouty arthritis

Dr Jeong Park, Institute of Molecular BioSciences, Massey University. TRRAP to GAS41: Potential roles of GAS41 in brain tumorigenesis

Prof Peter Little, Director of the Life Sciences Institute, National University of Singapore. Why are people different?

September

Kelly Prendergast, Malaghan Institute. How are langerin$^+$ CD8α^+ dendritic cells involved in systemic bacterial infections?

Prof Stewart Cole, École Polytechnique Fédérale de Lausanne, Switzerland. The ESX-1 system of *Mycobacterium tuberculosis* – structural and regulatory aspects

Emma Dangerfield, Malaghan Institute. The synthesis of glycolipids and azasugars to treat disease

Prof Ian Orme, Colorado State University, USA. Memory, immunopathogenesis and why TB vaccination is doomed to failure

October

Prof Bryan Williams, Director of the Monash Institute of Medical Research and Centre for Cancer Research, Victoria, Australia. Positive and negative regulation of innate immune signalling

Dr Kevin Francis, Caliper Life Sciences, and Kris Perano, Thermo Fisher Scientific. Preclinical *in vivo* imaging systems

Dr Stephen Daley, The Australian National University, Canberra, Australia. Eliminate or inactivate: the thymus as gatekeeper of the immune system

Dr Spencer Williams, University of Melbourne, Australia. Sweet medicine: molecular investigations into the roles of carbohydrates in disease and well-being

Kylie Price, Malaghan Institute. Flow Cytometry Tutorial: Controls

Carole Glynn, Director, Facilitating Research Co-operation between Europe and New Zealand (FRENZ). Presentation on the Marie Curie Fellowship opportunities available to New Zealand

November

Dr Ben Roediger, Centenary Institute, Australia. Transcription factor Ikaros dictates dendritic cell lineage choice in lymphoid and non-lymphoid tissues

Sach Jayasinghe, FlowJo, TreeStar Inc. FlowJo Tutorials

Dr Mahmoud Kiaei, University of Arkansas for Medical Sciences, USA. Nrf2/ARE signalling as a novel target for amyotrophic lateral sclerosis

Kelly Lundsten, Business Segment Manager for Advanced Cytometry, BioLegend, Santa Cruz, USA. Consolidating panels and expanding multicolour options in Flow Cytometry with the new Brilliant Violet Fluorophores

2012

January

Dr Kylie Quinn, Vaccine Research Center, National Institutes of Health, MD, USA. Comparative analysis of pox- and adenoviral vectors for CD8 T cell immunity

February

Dr Emma Ringqvist, AgResearch Hopkirk Institute, Palmerston North. Early interactions between the parasite Giardia and its human host – molecular studies of infection in an *in vitro* system

Prof Dan Eilat, Hadassah University Hospital Ein-Karem, Israel. B cell tolerance in autoimmunity: a change of concept is needed

Dr Lisa Connor, Malaghan Institute. Early dysregulation of the memory CD8α$^+$ T cell repertoire leads to compromised immunity to secondary viral infection

Prof Manfred Kopf, Molecular Biomedicine Institute of Integrative Biology, ETH Zurich. Understanding the development and function of alveolar macrophages by the identification of novel genes

Prof Manfred Kopf, Molecular Biomedicine Institute of Integrative Biology, ETH Zurich. Interleukin-21, a master regulator of T cell fate and function in allergies and chronic viral infection

Dr Andrew Clarkson, University of Otago. Cortical excitability and stroke recovery

Dr Takaharu Okada, Riken, Japan. Imaging of lymphocyte dynamics during the germinal center formation in the lymph node

March

Dr Troels Petersen, Malaghan Institute. Building potent cancer vaccines

Prof Keith Grimwood, Director, Queensland Children's Medical Research Institute, Brisbane, Australia. Rotavirus disease and its prevention

Dr Steven Bird, University of Waikato. How much have we learnt about the immunology of lower vertebrates?

Dr Ivan Biros, GE Healthcare Cell Technologies Leader. How cellular imaging just got redefined

Dr Joel Ma, University of Melbourne, Australia. Single cell gene analysis of HSV infected neurons

Prof JoAnne Flynn, University of Pittsburgh, PA, USA. Latent tuberculosis: a moving target

April

Rene McLaughlin, Malaghan Institute. Uric acid: more than just a risk factor for gout

Marcel Pronk, Vital Diagnostics. InKnow Dako: Research sector seminar

Dr Elizabeth Forbes-Blom, Malaghan Institute. Unplugging food allergy: understanding the cellular mechanisms underlying food allergen sensitisation

Prof Paul Klenerman, Nuffield Department of Clinical Medicine, University of Oxford, UK. Hepatitis C – immune responses and vaccines

May

Prof Philip Darcy, Peter MacCallum Cancer Centre, Melbourne. Preclinical development of gene-modified effector cells for the treatment of cancer

An Tan, Malaghan Institute. Is glucose addiction necessary for tumour metastasis?

Dr Bridget Stocker, Malaghan Institute. Chemistry, Immunology & Sugars

June

Stefanie Steiger, Malaghan Institute. Neutrophil cannibalism and inflammatory resolution via TGF-β1

Dr Patries Herst, University of Otago, Wellington. High dose vitamin C kills cancer cells in more ways than one

Mr Martin Hunn, Malaghan Institute. Snark or Snipe? – The hunt for a more effective vaccine for high grade glioma

Dr James Baty, Malaghan Institute. Silence of the LAM

July

Brigitta Mester, Malaghan Institute. Cell sorting at MIMR (technical seminar)

Isaiah Hankel, FlowJo. Flow cytometry data analysis seminars: Basic functionality, groups layouts, tables, batching and Compensation, transforms, advanced analysis platforms

Prof Antony Braithwaite, Dunedin School of Medicine, University of Otago. Isoforms of the p53 tumour suppressor and cancer

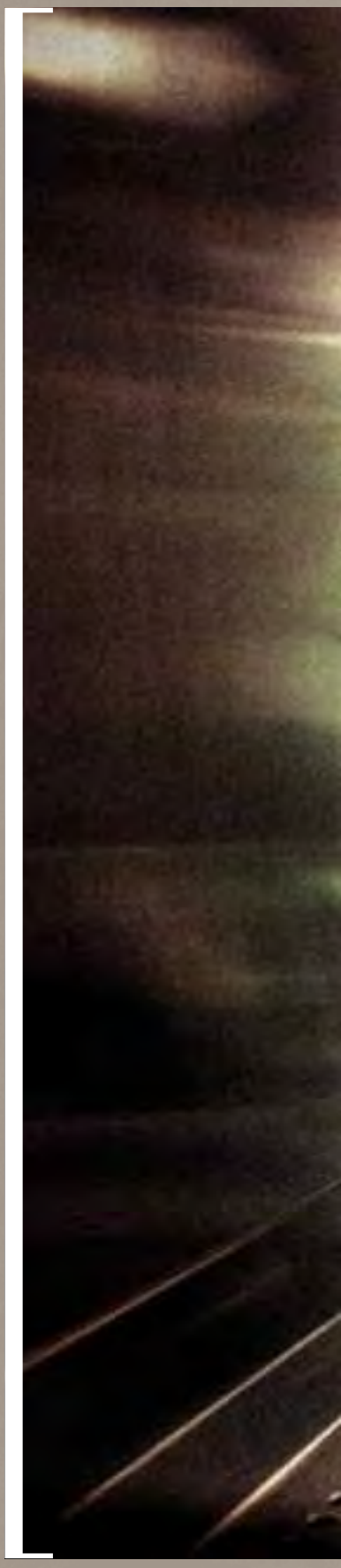
Prof Alan Musgrave, Department of Philosophy, University of Otago. Strict empiricism versus explanation of science

Operations & Governance

The Malaghan Institute is a charitable trust with tax-exempt status.

With no host organisation or direct government funding, we rely on fully-costed grants and public donations to support our research programmes.

The Trust Board provides the Institute with strategic guidance and oversight, while the management of the Institute is overseen by Director Prof Graham Le Gros.



› Evelyn Bauer.

Trust Board Profiles

MR GRAHAM MALAGHAN, ONZM, FCILT, Hon. DSc (VUW) **(Chairman)**

Appointed Chairman of the Malaghan Institute Trust Board in 1990. Commenced employment at General Foods Corp in 1967, and was appointed General Manager of Refrigerated Freight lines in 1970, acquiring the company in 1987. Was founding Chairman of Tasman Express Line and a member of the LTSA for six years. In 2009 was awarded an Honorary Doctor of Science from Victoria University of Wellington for his key role in rebuilding the Malaghan Institute into the largest independent medical research organisation in New Zealand. Current directorships include several private companies.

MR JOHN BEATTIE LLB (VUW)

Obtained a law degree from Victoria University (1975) and was a Fulbright Scholar to Cornell University (1979). Has been a Trustee of the Malaghan Institute since 1988 and is a Director of Malcorp Biodiscoveries Limited, a subsidiary of the Malaghan Institute, is also Chairman of the NZ Diabetes Foundation and the NZ Sports Hall of Fame. He is a Trustee of the Wanaka Festival of Colour and an Executive Director of the Infinity Investment Group along with directorships in Riverstone Holdings Limited and Pegasus Town Limited. He has been a partner in national law firm Kensington Swan, General Manager of Brierley Investments Limited and was the co-founder of Genesis Research & Development Limited with Jim Watson another Trustee of the Malaghan Institute.

PROF DAVID BIBBY DSc (Loughborough University)

Appointed to the Malaghan Institute Trust Board in December 2004. Is currently Pro Vice-Chancellor & Dean of the Faculty of Science, Pro Vice-Chancellor of the Faculty of Engineering, and Pro Vice-Chancellor of the Faculty of Architecture and Design at Victoria University of Wellington. Holds a PhD in nuclear chemistry and was awarded a DSc in 1995 for his research into zeolites and catalysis. Moved to New Zealand in 1975 to join the DSIR Chemistry Division where he became Group Manager Research before joining Industrial Research Ltd in 1992, initially as General Manager of Communications, Electronics and IT and then as General Manager of Science Development. In 2003, he took up his present position at Victoria University of Wellington.

ASSOC PROF JOHN CARTER BMedSc, MBChB(Otago), FRACP, FRCPA

Joined the Malaghan Board of Trustees in 2003. Did postgraduate work at the Fred Hutchinson Cancer Research Centre and the University of Washington. Clinically practices as a haematologist with a focus on stem cell transplantation. Is the immediate past Chair of both the New Zealand Blood Service and Scots College, and is currently Medical Leader of the Wellington Blood and Cancer Centre and an Associate Professor of the University of Otago.

PROF PETER CRAMPTON MBChB, PhD, FAFPHM, MRNZCGP

Appointed to the Malaghan Institute Trust Board in 2008. Is currently Pro-Vice-Chancellor of the Division of Health Sciences, and Dean of the Faculty of Medicine, for the University of Otago. Is a specialist in public health medicine with his research focused on social indicators and social epidemiology, health care policy, and health care organisation and funding.

MR BRYAN JOHNSON BCA (VUW)

Appointed to the Malaghan Institute Trust Board in 1998. Obtained a commerce degree from Victoria University of Wellington in 1963. Was a senior partner in the Stockbroking company Jarden & Co for 25 years and became Chairman after the sale of the business to Credit Suisse First Boston in 1991. Retired from CSFB in December 2000 to further develop his Marlborough winery and vineyard, Spy Valley. Has been a director of various corporations, such as Brierley Investments, Royal Sun Alliance and recently retired as Chairman of the Duke of Edinburgh's Award and was a Trustee of the Wellington Stadium Trust.

PROF GRAHAM LE GROS

BSc(Massey), Dip Immunol(Otago), MPHIL (Auckland), PhD(Auckland), FRSNZ

Appointed to the Malaghan Institute Trust Board in 1995. Was awarded a Fogarty Fellowship at the NIH, Washington DC in 1987-1989, then took a scientist position with Ciba-Geigy in Basel Switzerland for five years before returning to New Zealand to take up the appointment as Research Director of the Malaghan Institute in 1994. Is a Professor of the Department of Biological Sciences, Victoria University of Wellington, and has been elected as a Fellow of the Royal Society of New Zealand.

MR MATTHEW MALAGHAN

BCom

Appointed to the Malaghan Institute Trust Board in August 2008. Graduated from Otago University in 1994 with a Commerce degree. Subsequent employment with Refrigerated Freight Lines in Auckland and Melbourne, and Sea Containers Group in London, Madrid and Buenos Aires. Owns and operates property and mineral processing businesses in New Zealand and Australia. A Director of the Perlite Institute (USA). Member of the NZ Institute of Directors.

MR DAVID MOSSMAN,

QSM, BVSc, MRCVS, MNZIF

Appointed to the Malaghan Institute Trust Board in 2005. Attended Lincoln College and then graduated from the University of Queensland in 1965 with a Veterinary Degree. Awarded the Australian College of Veterinary Scientists college prize in 1978 and in 1984 the Coopers NZ Farm Management Award for significant innovative farm management in New Zealand. Keynote speaker at the World Angus and Hereford Conferences. A Member of the Lindisfarne College Board 1981-85. Managing Director of private Farming, Forestry, Finance and Property Companies. Chairman of the Hawkes Bay Friends of the Malaghan Institute since 1999 and retired rural veterinarian since 2001.

MR GARY QUIRKE

BCA, CA, FCILT

Appointed to the Malaghan Institute Trust Board in 2001, when he was Managing Director of P&O Nedlloyd in New Zealand. Has an extensive background in the commercial sector both in New Zealand and overseas and is a member of the Institute of Chartered Accountants and Fellow of the Chartered Institute of Logistics and Transport. Is currently involved in business management consultancy roles in service industries and Chairs a number of community based Boards.

DR JIM WATSON

PhD (Auckland)

Appointed to the Malaghan Institute Trust Board in 1993. Has been the Chief Executive of Genesis Research & Development Corporation Limited, (1997-2004), a company he co-founded in 1994. Has held Professorships at the University of California, Irvine (1976-1981) and the University of Auckland (1981-1993) serving as Head of the Department of Molecular Medicine (1983-1993). Was a Director of the Foundation for Research, Science and Technology (1999-2002), President of the Australasian Society of Immunology (2001), the President of the Royal Society of New Zealand (2003-2006) and a Member of the Government's Growth and Innovation Advisory Board (2001-2004). Is currently Chief Executive of Caldera Health Limited, a prostate cancer company.

MR C DAN WILLIAMS CA

Appointed to the Malaghan Institute Trust Board in 2005. Joined an antecedent firm of Deloitte in 1958 and following four years with the firm in London was admitted as a Partner in 1972, initially as the partner responsible for establishing the tax division and following that as a Business Advisory Partner. Retired in 2001 and is now a Consultant to the firm. Has a number of Private Company Directorships with emphasis on financial management.

Carolyn Hallsmith, Apii Ulberg, Marie Armstrong, Dominique Hawinkels, Michal Zablocki, Darrell Smith.

The Science Support Teams

ADMINISTRATION

PA to Director and Human Resources:
Gabrielle Dennis RSA(English), Pitmans

Purchasing Coordinator:
Carolyn Hallsmith

BRU

Manager:
Hannah Larsen BSc(Hons)(Queensland)

Training and Operations Manager:
Charlotte Cheriton

Senior Research Assistants:
Ian Saldanha BSc, PGDipSci(Otago), DipVetNursing(Otago Polytech), Xiaodong Wang Dip Med Tech, Dip Midwifery(Shanxi), Kelly Locke-Nelson, Laura McVeigh BSc(Hons)(Leeds, UK)

Research Assistants:
Victoria Long BSc (VUW), Lucas Pitt BMedSc(VUW), Bradley Rose BSc (VUW), Patrick Cavanagh BSc(Hons)(VUW), Ashlie Price BSc(VUW)

OPERATIONS

Chief Operating Officer:
Michal Zablocki BA(Hons)(Bristol), PGDipBA(VUW)

Facilities Manager:
Darrell Smith MSc(Hons)(VUW), (Dip A.T.) (Wgtn Polytech), BSA(Massey), Cert Building Mgmt(VUW), Electrical Applied Service Cert(WelTec)

Security and Reception Manager:
Dominique Hawinkels NZCS, DipBusStudies(Massey)

Systems Administrator:
Andrew Hamer-Adams

IT Support Technician:
Marie Armstrong BAP

Operations Laboratory Assistants:
Chris Covich, Laurence Fallon

Domestic Services:
Apii Ulberg

Operations Report

Success in research depends on the quality of the people involved; more so even than technology, funding or facilities. The same is true for research support and in this area the Malaghan Institute is particularly fortunate. This year I would like to focus on the individuals in our Operations team - talented and committed people who have dedicated years to furthering the Institute's goals.

Dominique Hawinkels has done almost every job in the place during his 21 years here, including working in the laboratories. He is now the friendly face in reception, who also happens to develop many of our databases in his downtime. Carolyn Hallsmith, a relative rookie with only six years at the Malaghan, combines reception work with procurement, finance, and occasional phlebotomy.

Darrell Smith knows every nut and bolt of the Institute. Another veteran from the old days, Darrell used to build our laboratories by hand. These days he is more likely to coordinate teams of contractors but has never lost his hands-on approach, can-do attitude or encyclopaedic knowledge of the facility.

Apii Ulberg has been working with us since we relocated in 2004. Her dedication, helpfulness and sunny disposition are a constant example for us all.

Marie Armstrong is a recent addition to the team, our latest geek in residence who supports our ever-expanding Information Technology platform with a calm and patient hand.

This year I celebrate my own ten-year anniversary at the Institute. That is a long time to spend with a single employer these days and it gives me pause to consider the surprising length of service from the members of this team. Essentially I believe it is because working in medical research is a privilege and this leads to a welcome symbiosis. They consider themselves fortunate to have the opportunity to support such important work; the Institute is fortunate to retain such a capable and dedicated team.

Michal Zablocki
CHIEF OPERATING OFFICER


MALAGHAN
INSTITUTE

Finance Report

Aimee de Koning, Susie Whelan, Janine Gray.

THE YEAR IN BRIEF	2012	2011
Operating Income ($000)	7,452	6,751
Operating Expenditure ($000)	7,652	7,249
Net Operating Deficit (before Depreciation)	(200)	(499)
Number of staff	56	56
Number of students	21	24
Total staff and students	77	80

THE FINANCE TEAM

Finance Manager:
Susie Whelan CA, NZIMDip

Assistant Accountant:
Janine Gray BCA(VUW)

Financial Accountant:
Aimee de Koning CA(VUW)

The Finance Department of the Institute connects all the areas of the Institute's activities and as such is tasked with providing information to Trustees and Trustee subcommittees, to ensure good governance and appropriate strategic development of the Institute.

Similarly, the Senior Scientists and Departmental Managers need accurate information on the status of the grants, the rate of spend, and a means for tracking the multitude of subcontracts, split funding and co-funding arrangements that have had to be developed for the support of staff salaries and research programmes. In addition the Finance Department needs to provide the Director with the appropriate management tools to ensure there is a good grasp of keeping the institute to budget and that the necessary financial planning for the replacement of infrastructure occurs. Lastly finance manages payroll, funds and investments.

In order to carry out these tasks, we receive the support of Deloitte who conduct our annual audit and offer advice on our accounts. First NZ Capital provides pro-bono advice on the management of our investment portfolio.

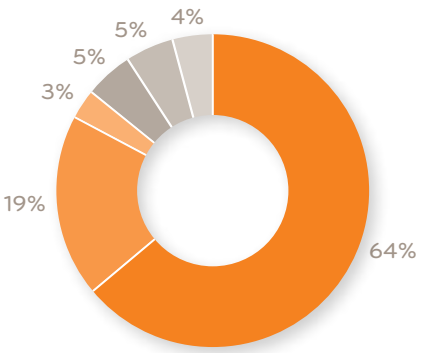
Internally, our department is supported by an Audit and Finance subcommittee of the Trust Board, which both acts as a sounding board and ensures that the Institute does not overstretch its financial resources so that we can continue to provide the facilities that support research.

My team of three strives to provide an easy interface for all staff to be able to access the information when required and in an easy to use format. At the same time we endeavour to get the best from our financial systems in an increasingly complex regulatory and operationally demanding environment, which is evolving rapidly.

We are ready to continue to provide financial information to all our customers in the next financial year to enable the Institute to fulfil its strategic vision.

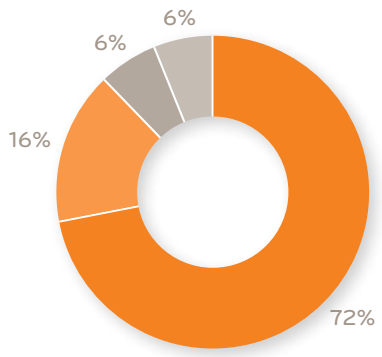
Susie Whelan
FINANCE MANAGER

Financial Overview



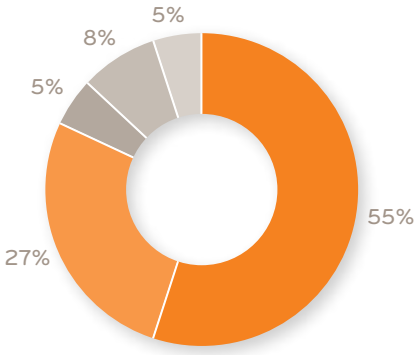
INCOME

	Contestable Grants – Government
	Contestable Grants – Non-Government
	Other Funding
	Donations
	Bequests
	Investment Income



EXPENDITURE

	Science
	Laboratory Support
	Development & Communications
	Administration



STAFF NUMBERS – HEADCOUNT

	Science
	Science Students
	Laboratory Support
	Development & Communications
	Administration

Financial Overview – Performance
For the Year Ended 31 July

	2012 CONSOLIDATED	2011 CONSOLIDATED
Income – Operating		
Donations	461,837	440,375
Scientific Grants	6,728,551	6,090,430
Sundry	261,209	219,990
	7,451,597	**6,750,795**
Expenses – Operating		
Salaries	3,984,960	3,993,337
Science & Laboratory Support	3,411,190	2,999,308
Other	255,876	256,794
	7,652,026	**7,249,439**
Operating (Deficit)	**(200,429)**	**(498,644)**
Income – Other		
Grant Income	515,600	265,340
Capital Endowment Fund - Investment Income	264,462	507,208
Capital Endowment Fund - Bequests	415,895	333,167
Research Reserve transfer	17,706	46,979
Income retained in Capital Endowment Fund	53,878	(418,246)
	1,267,541	**734,448**
Depreciation	(453,018)	(472,950)
Net surplus/(Deficit)	**$ 614,094**	**$ (237,146)**

Financial Overview – Position
As at 31 July

	2012 CONSOLIDATED	2011 CONSOLIDATED
Current Assets	4,049,456	2,254,511
Current Liabilities	(4,367,405)	(3,096,866)
Working Capital	**(317,949)**	**(842,355)**
Fixed Assets	1,478,581	1,406,594
Investments	5,426,845	5,480,728
Total Equity	**$ 6,587,477**	**$ 6,044,967**

Additional Acknowledgements

In addition to the staff of the Malaghan Institute who are listed throughout this Annual Report, we would also like to acknowledge the following people and organisations who are very generous in giving their time and expertise to support our operations.

RESEARCH AND CLINICAL CONSULTANTS

Adjunct Prof Richard Beasley, University of Otago

Assoc Prof John Carter, Wellington Blood & Cancer Centre and University of Otago

Prof Brett Delahunt, University of Otago

Dr Peter Ferguson, Wellington Hospital

Dr Michael Findlay, Cancer Trials NZ, University of Auckland

Prof Andrew Harrison, Dept of Medicine, Wellington School of Medicine & Health Sciences

Dr Rebecca Grainger, Hutt Hospital

Assoc Prof David Ritchie, Peter MacCallum Cancer Centre, Melbourne, Australia

INDEPENDENT SCIENCE REVIEW PANEL

Prof Ashley Dunn (Chair), Former Associate Director of the Ludwig Institute and Fellow of the Australian Academy of Science

Assoc Prof John Carter, Wellington Blood & Cancer Centre and University of Otago; former chair of the New Zealand Blood Service and Malaghan Institute Trustee since 2003

Prof Peter Little, Director of the Life Sciences Institute, National University of Singapore and former Research Director of UNSW, Asia

Prof Ranjeny Thomas, Diamantina Institute, University of Queensland. Founder and Director of Dendright

Prof Bryan Williams, Director of the Monash Institute of Medical Research and former chair of the Department of Cancer Biology at the Lerner Research Institute

ADVISERS

Auditors	Deloitte
Bankers	The National Bank
Investments	First NZ Capital – Chris West & Ralph Goodwin
Solicitors	Simpson Grierson

Taryn Osmond.

Community Engagement

Research takes dedication, passion and drive. Supporting the research undertaken at the Malaghan Institute takes a special type of person. We are proud of the people that get involved with us and partner us on our journey.

Our network of donors, sponsors and volunteers allows us to continue the necessary work we do and we are eternally thankful for all of these partnerships.

Tanya Fulcher, Jacqui Whelan, Viv Bernard, Dr Debbie Scarlett, Jenny Sim.

Development Report

People and relationships are the most important factors for the Development team, which may seem like an odd thing to say, given that our mandate is to ensure continued supported funding of the Malaghan Institute. But this task comes down to these two very important things and we are the fortunate team that converses with the individuals, trusts, volunteers and organisations that contribute funds to our research.

The one thing we have learnt from these conversations is that every donation comes with a story, every bequest a memory and every grant comes with a hope. It is the Institute's responsibility to live up to these hopes and be good stewards of this funding. This year a lot has been done to ensure we're meeting research targets; nationally and internationally; and using any investments wisely, and we'd like to thank the Trust Board for having a steady hand on the tiller while the New Zealand economy has been passive. We know that the work we do bringing funding into the Institute is well supported by them.

> "…every donation comes with a story, every bequest a memory and every grant comes with a hope."

The other group of individuals to mention is my Development Team. They are; **Tanya Fulcher** – *Operations Manager*; **Dr Debbie Scarlett** – *Science Communications Adviser*; **Victoria Hale** – *Marketing and Relationship Manager*; **Jacqui Whelan** – *Fundraising Assistant*. We also said goodbye to **Angela McGuigan** in June, and welcomed **Jenny Sim** to the team in July - to cover for Tanya as she goes on maternity leave. Their dedication and support ensures we deliver great results for the Institute.

Finally the most important relationship that we value is the one with our supporters. This support comes in many different forms and without it the research would stop, so thank you very much to all of you who have shown your commitment to our Institute this year.

Below are some highlights from this year:

- Our dedicated Friends Groups raised over $115,000 by holding their annual charity golf days, as well as a fashion event and Love Boat Ball.
- Over 390 visitors came through the doors for a tour of the Institute.
- We spoke at 11 events and reached over 540 listeners.
- Over $175,000 was received in donations via our direct mail appeals. To reach this outstanding total, over 2,100 individual donations were generously given.
- Run for Research attracted 13 teams and over 120 participants, had the support of 32 volunteers and raised over $35,000.

Thank you for your stories, your memories and your trust that we will deliver on your hopes.

Viv Bernard
NATIONAL DEVELOPMENT DIRECTOR

THE DEVELOPMENT TEAM

National Development Director: Viv Bernard

Development Operations Manager (P/T): Tanya Fulcher, BSc(VUW)

Marketing & Relationship Manager (P/T): Victoria Hale, BCA, BSc(VUW)

Science Communications Adviser (P/T): Dr Debbie Scarlett, BSc(Hons), PhD(Otago)

Fundraising Assistant (P/T): Jacqui Whelan

To June 2012: Marketing & Administration Assistant (P/T): Angela McGuigan

From July 2012: Fundraising Operations Manager: Jenny Sim

Community Engagement

As well as conducting ground-breaking research into cancer, asthma and allergy, arthritis, MS and infectious disease, a key goal of the Malaghan Institute is to educate and raise awareness within the community about the importance of medical research. One way that this is achieved is by engaging with the community through tours, science talks, events and media.

The following provides an overview of our community activity during the 2011/2012 period:

TOURS

Chilton Saint James School

Chinese People's Liberation Army

Kelburn Brownies

Lions Club of Kapiti

Malvina Major Retirement Village

Ole Football Academy

Paramata Probus Club

Petone Combined Probus

Rotary Club of Harbour City

Various MP and individual visitors

VUW Study at Vic Day

Wainuiomata Senior Citizens Group

Wairarapa College

Whitireia New Zealand

SPEAKERS

Combined Probus Club of Paraparumu Beach

Eastbourne Lions Club

Hutt Arthritis Exercise Group

Hutt Valley High School

Lions Club of Kapiti

Probus Club of Heretaunga

RNZCGP Education Committee - GP CME Meeting

U3A Wellington City Inc.

Z Energy

EVENTS

2012 AMI Round the Bays - Run for Research

Centre for Brain Research, University of Auckland - Brain Day 2012 (expo stand)

Malaghan Open Day for VUW students

Pah Homestead Cocktail Evening

VUW Science Careers Expo (expo stand)

ONLINE FUNDRAISERS

We would also like to acknowledge the efforts of some inspiring people who have run their own event and raised money online in support of the Malaghan Institute:

- Harriet Small & Catherine Tomlinson - Harry and Kat shave their heads
- Maureen Archer - Everest Marathon
- Greig Rightford & William Tokona – Be Smart Sahara Charity Challenge

MEDIA

Our scientists, research and fundraisers have also featured in local, national and international media including: the Dominion Post and Sunday News; community and regional newspapers; magazines such as Australian Life Scientist, Good Magazine, National Business Review, New Zealand Listener, North & South and Pharmacy Today; radio interviews on Newstalk ZB, Radio Live and Radio New Zealand; online including NZ Herald, Stuff, 3 News, and TV broadcasts including TV One Breakfast Show and TV One Special Report.

If you are interested in finding out more about our tours, speakers or events please contact:

Victoria Hale: Marketing & Relationship Manager, +64 4 499 6914 ext. 821, vhale@malaghan.org.nz

Fundraising Highlight

RUN FOR RESEARCH

What a sight it was to see over 12,000 people line Jervois Quay in Wellington on Sunday 26 February for the sell-out 2012 AMI Round the Bays!

This year our involvement in this event was taken to a whole new level after being announced as the event's new Official Charity Partner, providing an excellent opportunity to reach the wider community and raise awareness of the Malaghan Institute in addition to raising important funds.

The Run for Research brought together people of all ages, from all walks of life and fitness levels, united by their motivation to get behind a great cause and support the work of the Malaghan Institute. Over 120 people took part in the Malaghan Institute Run for Research and an additional 160 people took part as Malaghan Charity Runners, all helping to raise over $35,000 to support our research.

This year also marked the beginning of a great partnership between the Malaghan Institute, AMI Insurance and Sport Wellington, and it was fantastic to have the opportunity to get the Malaghan name out there and associated with such a well known and loved community focused event.

We received support from world renowned Wellington runner Melissa Moon as the Run for Research Ambassador, the team at Clemenger BBDO who worked with us on the campaign and promotion, Lexus of Wellington who loaned a Lexus RX SUV as a promotional vehicle and Z Energy who provided fuel to ensure the Run for Research vehicle received as much exposure as possible on the roads of Wellington.

We were humbled by the enthusiasm and dedication of the individuals and teams who took part in the Run for Research and the support of those in the community who donated. Thank you to everyone involved for making the 2012 Run for Research such a great success!

Melissa Moon.

"Every step brings us closer to a cure"

- As the Official Charity Partner of AMI Round the Bays we were able to get our message out to 12,000 participants.
- $35,000 was raised in total; over $30,000 from Run for Research and over $4,500 from our Charity Runners.
- 13 teams and over 120 individuals ran or walked for us as part of the Run for Research, and over 160 people took part as Charity Runners.
- A Run for Research branded Lexus RX SUV promoted the Malaghan Institute around wider Wellington.

principal supporter AMI · sport Wellington · CLEMENGER BBDO · LEXUS OF WELLINGTON · Z ENERGY

Three generations support the Run for Research

Taking part in the 2012 Malaghan Run for Research and raising over $1,000 meant something very special to Wellingtonian Marie Gillies.

Ranging in age from nine to 68 years, Marie, along with her two daughters and two granddaughters walked the 7km around the bays of Wellington together in memory of their beloved husband, father and grandfather, Bob, who died of cancer.

Bob was a fit and active 69 year old, still working and enjoying life when he was diagnosed with lymphoma in November 2010. He sadly passed away a mere four months later, on 27 March 2011.

"For us as a family, this was a difficult and shocking time and it is only through continuing research into cancer, that treatments can improve, and who knows, maybe a cure will be found," says Marie.

"It was our pleasure to take this small opportunity to help support the important research work the Institute does."

Run, walk or crawl the distance

Carol Price of Whitianga is another inspiring individual who joined the 2012 Run for Research. At 67, Carol had lived with rheumatoid arthritis for more than 16 years. She says that AMI Round the Bays gave her the incentive to get back to running by having something to commit to, and she was driven even more by the desire to raise money to support research along the way. Not only was her commitment shown by the distance she travelled to take part, but also by her determination to complete the 7kms whether she "ran, walked or crawled the distance".

JOIN US IN 2013!

There are many ways that you can support the Run for Research:

- Participate and fundraise as an individual, family, group of friends or corporate team
- Sponsor someone taking part
- Volunteer

For more information contact:
Victoria Hale: Marketing & Relationship Manager,
+64 4 4996914 ext. 821,
vhale@malaghan.org.nz

Friends of the Malaghan Institute

The Malaghan Institute is very fortunate to have the support of five regional volunteer Friends committees. These wonderful people work extremely hard on our behalf, not only to raise funds for our work, but also to raise overall awareness of the Malaghan Institute. Our sincere thanks go to these amazing people who give their time to our cause.

WELLINGTON COMMITTEE

Susan Laurenson (Chair)
Judy Blair
Adrienne Bushell
Maureen Cameron
Eleanor Harford
Jennie Johnstone
Jill Kinloch
Emma Lawler
Fiona Matthews
Fleur Stewart
Denise Udy
Jane Wilton

Wellington Events

Lexus of Wellington Malaghan Institute Charity Golf Tournament [1]

HAWKES BAY COMMITTEE

David Mossman (President)
Denise Bull (Chair)
Margie Dick
Beth Kay
Bry Mossman
Andy Neilson
Rosemary O'Connor
Jan Paterson
Angie Piper
Kathy Rittson-Thomas
Bruce Speedy
Lynn Spence
John Stovell
Terry Thornton
Graeme Wedd

Hawkes Bay Events

Malaghan Institute Charity Golf Tournament [2]

AUCKLAND COMMITTEE

Matthew Malaghan (Chair)
Margaret Malaghan
Lindsay Bradfield
Mary Collow
Trudi Gardner
Elaine Haggitt
Alison McKenzie
Deborah Malaghan
Jane Parlane
Raewyn Roberts
Julie Sobiecki
Greg Shepherd

Auckland Events

Malaghan Institute Charity Golf Tournament [3]
Love Boat Ball

TAUPO COMMITTEE

Anne Velvin (Chair)
Merryn Herrick
Caroline Martin
Kathryn Uvhagen
Rick Whitlock
Adele Wilson
Doug Wilson

Taupo Events

Charity Fashion Show

WAIRARAPA COMMITTEE

Campbell Moon (Chair)
Sally Campbell
Debbie Clinton-Baker
Michael Clinton-Baker
Mary des Bonnets
Gretel Dick
Joy Mebus
Jill Moon
Barbara Sheehan
Ted Sheehan

Wairarapa Events

Antiques Roadshow

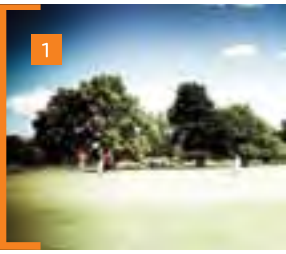

2


3


2


1


1


1


3


3


1


2


2

Funding Sources

Thank you to the following individuals, organisations, businesses, Trusts and Foundations who helped support the Malaghan Institute from 1 August 2011 – 31 July 2012:

Grants, Trusts and Foundations

AgResearch Ltd, Hamilton
Arthritis New Zealand
Arthur N Button Charitable Trust
BEA Trust
Cancer Society of New Zealand (National Body and Wellington Division)
Carol Tse (No 2) Family Trust
Child Health Research Foundation
E M Pharazyn Charitable Trust
F H Muter Charitable Trust
Fonterra Co-operative Group Ltd
Genesis Oncology Trust
H B Williams Turanga Trust
Health Research Council of New Zealand
Hugh Green Foundation
Industrial Research Limited
Infinity Foundation Limited
Just Paterson Real Estate Ltd
Keith Seagar Research Fund
Margaret Neave Charitable Trust
Maurice Wilkins Centre for Molecular Biodiscovery
Melanoma Research Alliance
New Zealand LAM Trust/LAM Australasia Research Alliance
New Zealand Lottery Grants Board – Health Research
Rex & Betty Coker Foundation
S E Leuchars Family Trust
Springhill Charitable Trust & Frimley Foundation
Sugar Charity Ltd
The Dr Marjorie Barclay Trust
The Estate of W J Thomson
The Graham Hall Bequest
The Great New Zealand Trek Charitable Trust
The Levene Foundation
The Margaret Ann Tibbles Charitable Trust
The Neurological Foundation of New Zealand
The Nick Lingard Foundation
The Paddy Brow Charitable Trust
The Southern Trust
The Thompson Family Foundation, Inc.
The Trusts Community Foundation
University of Otago
Wade Thompson
Wellington Medical Research Foundation

Bequests

The following people generously left bequests to the Institute:

Ivy Kathleen Berridge
Rayner Vincent Dixon
Alan McLean Duncan
P M Evans
E F Haslam
F J Hindmarsh
Ethel Reed Hitchen
Heather Kimber
P M Matthews
Vera McAloon
Bernard John Russell

Corporate Partners

AMI Insurance
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Dave Clark Design
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Lexus of Wellington
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Spy Valley Wines
Z Energy

Corporate Supporters

Aotea Pathology
BNP Paribas Security Services
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Wairoa Warrant of Fitness Centre

Special Donors

AMI Insurance Team - Over $1,000 raised for the Run for Research
Vivienne Apperley
Maureen Archer - Everest Marathon
George Austin
Anna Bidwill
E R Bidwill
Wyn Charlebois
A & J Cockburn
J W Dalmer
Ali Daniell
J Dougall
Mavis J Evans
Mary Fawcett - Over $1,000 raised for the Run for Research
Marie Gillies - Over $1,000 raised for the Run for Research
Cliff Grice
J Holdsworth
Milton Hollard
Bary Hollow - Over $1,000 raised for the Run for Research
S Iorns
Frances Lee
Lions Club of Parawai
M H Livingstone
Loyal Orange Lodge No 20
Matthew Malaghan - Over $1,000 raised for the Run for Research
Steve Marshall
Peter Martin
Karen McNeill
Huguette Michel-Fleurie
Oliver R Nees
Lester Oakes
Beverley Peach
R Pilgrim
Greig Rightford & William Tokona - Sahara Charity Challenge
Rotary Club of Port Nicholson
Rotary Club of Wellington
J C Saunders
Harriet Small & Catherine Tomlinson - Harry & Kat shaved their heads
Lynn & Alastair Spence
St Lukes Mission Guild
R W Stannard
Alison Tanner
Phil Taylor
C J Thompson
Colleen Thurston
C M Tisdall
N Todd
Helen Todd
W Tucker
John Turner
The 'W' Team/Cameron Family - Over $1,000 raised for the Run for Research
Sir James Wallace
Vivien Ward
Michael R Wilkes
C D Williams
Michael Woodside - Over $1,000 raised for the Run for Research
Z Energy Team - Over $1,000 raised for the Run for Research

In Memoriam

Donations were received in memory of the following people:

Joan Betteridge
Norman Bevan
Mrs Joan Campbell
Denise Dellabarca
Patricia Rae Edmonds
Mrs Dawn Gibson
Geoffrey Gill
Cyril Donald Hutchings
Helen Sinclair Lewis
Walter and Phyllis Matthews
Fiona Marian Niccol
Elizabeth Rose O'Connor
Bob Parker
Audrey Roberts
Harry Romanes
Yvonne Margaret Rose
Richard Rowell
Roger Edmund Smith
Gwen Sylvester
George Tanner
Nelson Craig Taylor
Ellen, Sinclair, Barbara and Alison Wallace
Caroline Wiggins
Gillian Wood

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Fliway International Ltd
Fonterra Brands (Tip Top) Ltd
Frank Pearson Investment Advisory Ltd
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Graham de Gruchy
Gresson Grayson Ltd
Hansen & Bate
HSBC
Ian Grieve
Industrial Processors Ltd
JBWere
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Loyalty NZ
Mick Ormond
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Onesource Ltd
Opus International
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The Levene Foundation
The Rivets
The Wallace Arts Trust
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Wairoa Veterinary services
Wairoa Warrant of Fitness Centre
Whakatu Coldstores Ltd
Whenuahou Station Limited
Woodlands Station
YOU Mens Health Trust

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Brittain Wynyard
Cable Bay Vineyard
Café L'affare
Cape Kidnappers
Chocolate Frog Café
Circa Theatre
Colin Blair
Craig Foss MP
Dan Hewitt
David & Bry Mossman
Delmaine Foods
Diva Restaurant & Lounge
Dymocks Books
Elements Café
Elizabeth Horne
Esteem Jewellery
Eurovintage
Farmlands Trading Society Ltd
Ferryman's Cottage, Martinborough
Floyds Restaurant
Fonterra Brands (Tip Top) Ltd
Forbes and Co
Fosters New Zealand Ltd
Frucor - H2GO
Fullers
Gallery Hair Design
Gannet Safaris Overland Ltd
Gerald Wilson
Glengarry Wines Thorndon
Grande Gourmet Ltd
Hastings Pro shop
Hawkes Bay Insurances
Haylo Skin and Body
Joanna Fleming
John Holt Memorial Trust
Johnson Estate
Kauri Cliffs Golf Resort
Kay Geor
Krystal Foss
Laserforce
Lauraine Jacobs
Laurie Harrison
Le Metropolitian
Lexus of Wellington
Loyalty NZ
Lynn and Alistair Spence
Malcolm Gourlie
Mark Howard
Martin Bosley's Yacht Club
Matangi Farm Cottage
Mike and Sally Blackmore
Millenium Hotels
Millwood Gallery
Museum Hotel
Nancy Tichborne
National Bank
New World, Havelock North
New Zealand Symphony Orchestra
Novotel, The Terrace
Obiqo
Off The Track Restaurant & Licensed Café
Olive Tree Café
Opus International
PakNSave, Hastings
Pak-line
Peak Horticulture Ltd
Peter Shirtcliffe
Random House Publishing
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St Martin Vineyard, Martinborough
Steve Smith
Strawberry Patch
Super Cheap Plumbing
Team McMillan BMW
Terrace Downs Resort
The Diamond Shop
The Gables Restaurant
The Make-Up and Nail Studio, Hataitai
Thomson's Suits
Tom's Cottage
Tracey Russell
Trevor Melville
Tunanui Farm Cottages
Turners & Growers
United Containers
Urban Retreat of Hastings
Urban Sanctuary
VetEnt Napier
Vet Services Hawkes Bay
VetEnt Wairoa
Veterinary Associates Hastings Ltd
Village Press
Vista Café
Waiheke Executive Transport
Walk Gisborne
Yummy Apples

How You Can Help

There are many things you can do to support the Malaghan Institute; from making a donation, to volunteering, to 'liking' us on Facebook. Our supporters believe that we are making a difference to the lives of New Zealanders and we invite you to be involved in this potential.

You can be sure whatever you do will contribute to our work and help us discover treatments and cures for cancer, asthma and allergy, arthritis, MS and infectious disease.

We are independent and receive no direct government funding. We are reliant on contestable research grants and contributions from corporate sponsors, trusts, bequests, individuals and fundraising initiatives.

The Malaghan Institute is at the forefront of international medical research, and our scientists believe that the key to fighting illness lies in the immune system. Our research programmes are focused on finding better treatments and cures for diseases affecting New Zealanders and without funding the work will stop and the goal will be unattainable.

We are a registered charity and any support is gratefully received. You can support our vision by investing in health for the benefit of all New Zealanders. The following are some options of how you can become involved:

Corporate Sponsorship

Corporate sponsorship enables the Institute to focus financial resources on core medical research and offers an opportunity to the corporate sector to enjoy the promotional benefits of being associated with the Malaghan Institute. We have several options for sponsorship including local and national events, laboratory naming rights and the procurement of specialist pieces of scientific equipment. We will recognise your support in a way that is appropriate to your organisation.

Donations

Donations from individuals and Trusts form a large part of our funding. The income is used to support the research programmes and are acknowledged by a personal letter and receipt. All donations over $5 are tax-deductible.

Bequests

The research at the Malaghan Institute is very dependant on bequests. We have developed an endowment fund that will grow from major gifts and bequests, hence sustaining the future of the Institute.

Following is a suggested format for the wording of a bequest.

"I give and bequeath to the Malaghan Institute of Medical Research,

- A percentage (%) of my estate or
- The following property and assets or
- The residue of my estate or
- The amount of $ (in words)

for its general purposes (or for the purpose of....) and I declare that the receipt of the chief executive or other proper officer shall be full and sufficient discharge to my trustees".

We would be delighted to discuss options for acknowledgement to suit your wishes.

Should you require any additional information about the above options or have any queries, please contact:

National Development Director

Malaghan Institute
of Medical Research,
PO Box 7060
Wellington 6242
New Zealand

P: +64 4 499 9614 ext. 895

Please visit www.malaghan.org.nz for further information.

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