Malaghan Institute of Medical Research

Annual Report 08

MISSION STATEMENT

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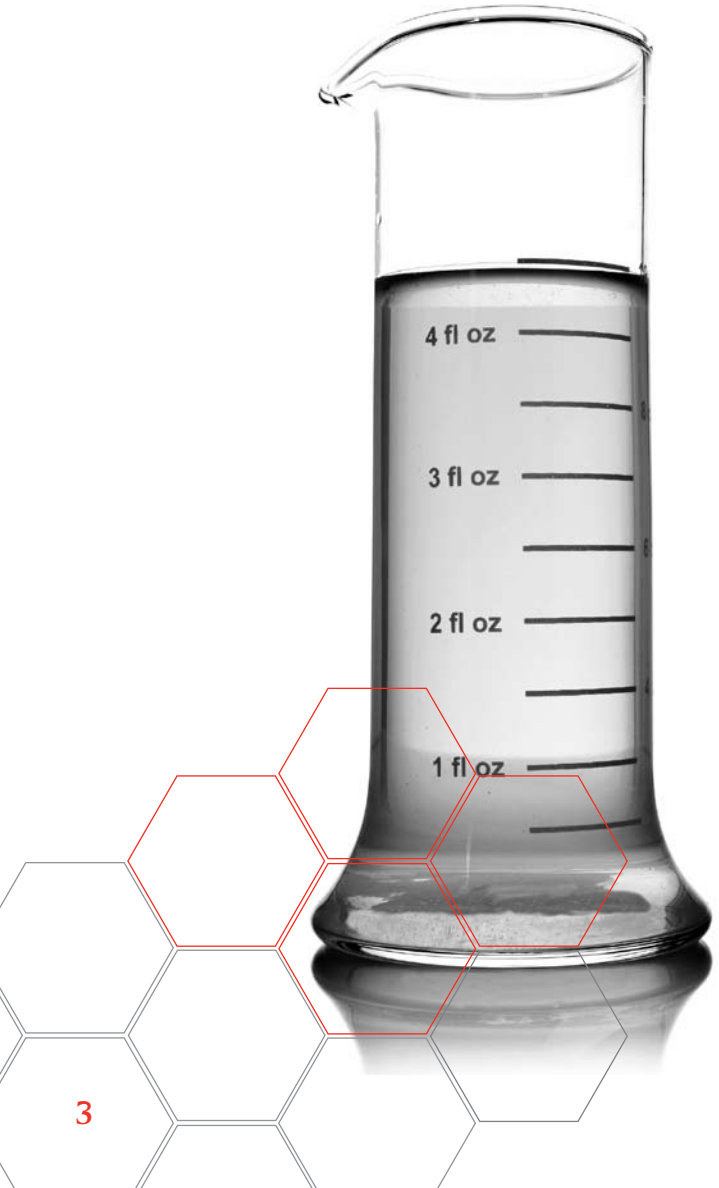


OVERVIEW

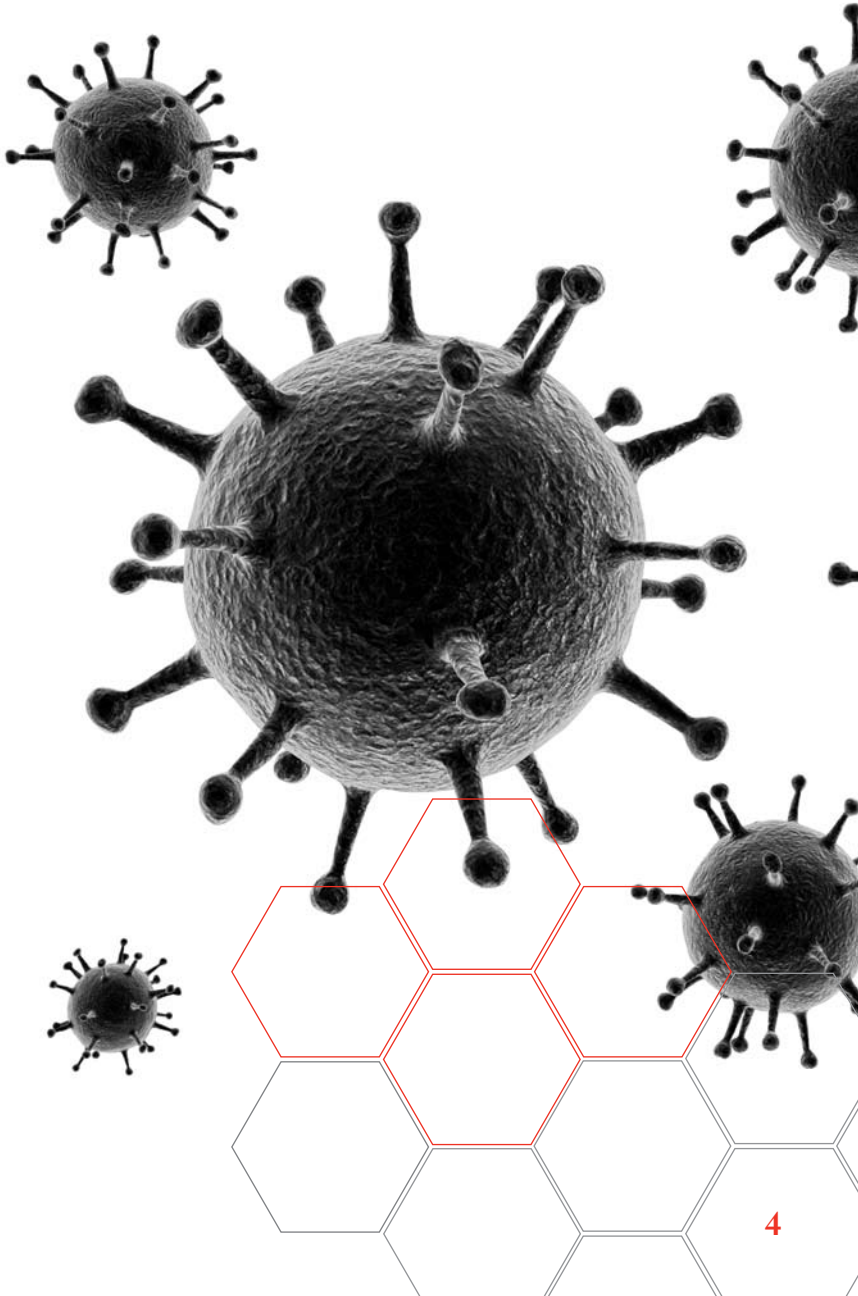
The Malaghan Institute is New Zealand's only independent medical research institute and is a charitable trust.

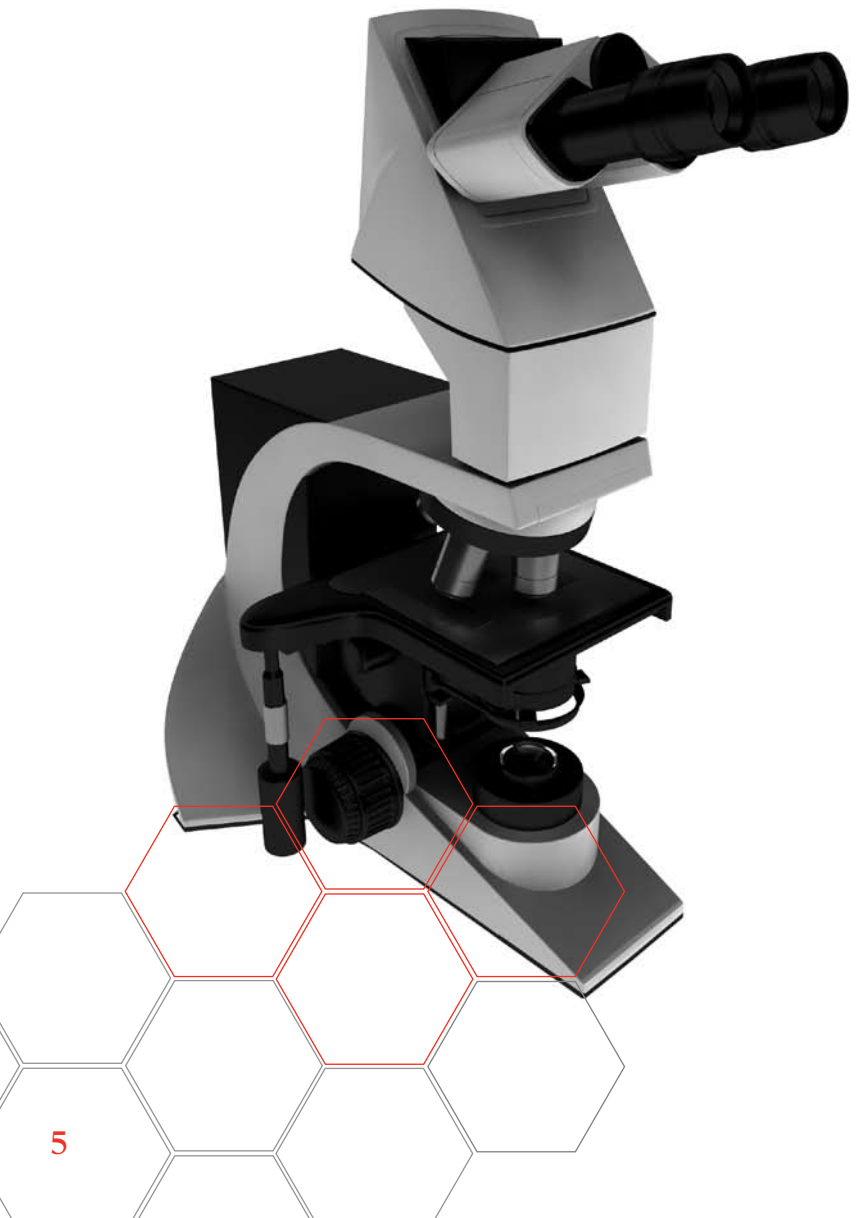
Our scientists are dedicated to the prevention and treatment of cancer, asthma, arthritis, multiple sclerosis and infectious diseases.

At the Malaghan Institute we believe that the key to fighting illness lies in harnessing the immune system, the body's own natural defence against disease. Increasingly we are able to apply new insights into how immune reactions are triggered and controlled at a molecular level, including clues for how specific aspects of the immune response are governed by the genes within cells. As we increase the depth of our understanding of the immune system the potential benefits for New Zealanders are limitless. In addition to our drive for making discoveries, the Institute is committed to the development of New Zealand scientists and clinicians.

The Malaghan Institute has an international reputation as a cutting-edge medical research and training facility, housing New Zealand's brightest and most creative scientists, doctoral students and post-doctoral fellows. To ensure that the vital research at the Institute persists, we rely on contestable grants, corporate sponsorship, trusts, bequests and donations.

Over the last 30 years, the Malaghan Institute has built an international network of collaborators and supporters who are helping us combat the diseases that affect New Zealanders. Working with these 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. On a national scale, the Institute works closely with tertiary institutions, Crown Research Institutes, hospitals and clinics throughout New Zealand at the same time preserving our independent status.





A five year plan has been developed and will be steered through its paces by a committee of both Trustees and Management.

Each year brings its own challenges and 2008 was no exception. The Director's Report gives a good account of the many events and successes that made up the year and those still in front of us.

Trustees have focused on the long-term funding requirements for the Institute, providing the infrastructure and resources necessary for our research teams to be successful.

A five year plan has been developed and will be steered through its paces by a committee of both Trustees and Management.

This plan calls for the establishment of additional Friends groups around New Zealand to grow awareness and to identify opportunities for fundraising. Growth of our Capital Endowment Fund, by attracting further gifts and Bequests, is the primary source and manner for supporting our research teams. The Trustees and the Director utilise the Fund to underwrite projects and to support the various scientific endeavours identified by the Director.

Over recent years we have been increasingly concerned at the vagaries and lack of strategic focus of science funding by the Government. Certainly in the area of health research this has been very true, where we compare poorly to similar economies such as Australia, USA and the European Union.

We did approach Government this year to contribute with us equally in the funding of a new Cell Therapy Centre and its operations. Regrettably however, we were advised that whilst we are highly regarded and

CHAIRMAN'S REPORT

that the project was exciting and cutting-edge, the Government would not take up the challenge of supporting us on a dollar for dollar basis.

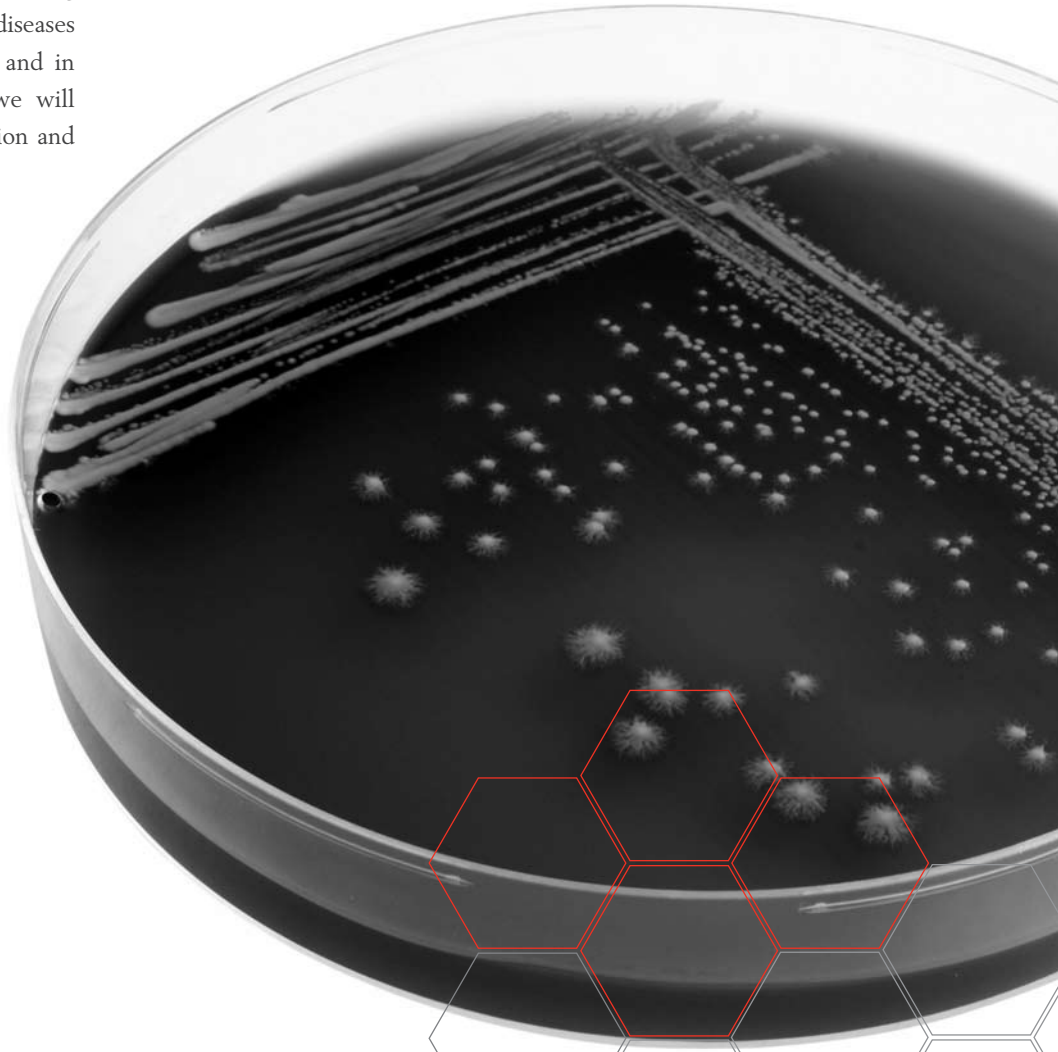
This was a very disappointing decision, made on the basis that adequate sources of existing Government funding were already available to support such a Centre. The fact that the CRI's and Universities with whom we compete for such funding are funded by Government to have the capacity and capability to support their grant applications, makes for a very unequal playing field. We will try again.

The Institute spends less than 15 cents in the dollar of the money raised and expended each year on administration and promotional costs; this means that 85 cents in every dollar goes directly to actual research activities.

The Director and Trustees are challenged by this achievement and remain focused to ensure that whilst we grow our profile we need to ensure that money raised continues to go primarily to the research that we promote for funding.

The Director has made a mention of the special relationship that we have with Victoria University; this has proven to be more supportive and responsive than we could have envisaged when we made a move to become a tenant on their Campus, some four years ago. This mutually beneficial relationship bodes well for the future of public and private partnerships in science.

Without the dedication and generosity of you and yours, we could not, as trustees and researchers, hope to continue the work of the Institute in discovering new approaches to prevent and treat the diseases in our communities. Our thanks go to you and in the more difficult economic years ahead we will endeavour to continue to engage your attention and support.



Graham Malaghan

CHAIRMAN

DIRECTOR'S REPORT

The Malaghan Institute faced a number of significant challenges in 2008. To ensure we retained our position as an internationally recognised independent medical research facility during these testing times, the Malaghan Institute scientific staff vigorously pursued the objectives of their individual research groups and the development of new original programmes of research relevant to their respective disease areas. I am pleased to report that the infrastructure and resources provided by the Institute have been able to support this effort very well, with a significant number of high impact scientific publications being produced for the year.

Our cancer research in particular took centre stage this year. In an important first the Malaghan Institute combined its expertise in immunology and oncology with the synthetic chemistry research institute, Industrial Research Limited (IRL), to unlock the enormous commercial potential of our cancer vaccine. Another significant development in our cancer research programmes in 2008 was our joining of a global collaborative Melanoma Research Alliance involving cancer researchers at the Malaghan Institute, the Ludwig Institute in Melbourne and research teams in New York and South Africa. For several years now, the Cancer Cell & Molecular Biology group has been developing models of the cancer stem cell for drug targeting and is now working with the Institute's Cancer Immunotherapy and Vaccine Research Groups to investigate immune responses against melanoma stem cells, in the hope of identifying novel antigens for use in our cancer vaccine protocol.

Complementing our melanoma cancer immunotherapy research is a recently launched phase I clinical trial in collaboration with Wellington Hospital neurosurgeon Mr Martin Hunn. This trial tests the feasibility and safety of using dendritic cell vaccines in combination with standard chemotherapy for the treatment of patients with the highly aggressive brain cancer glioblastoma multiforme. To maintain the continued success of our individualised cancer vaccine programme, it is our intention to establish a new Cell Therapy Centre at the Malaghan Institute, which will increase the existing capacity for delivering our cell-based therapies and provide resources for the extension of this novel and exciting technology to other forms of disease.

Unfortunately, our Multiple Sclerosis research programme was forced to undergo a complete restructuring this year with Group Leader Assoc Prof Thomas Bäckström leaving to take a senior position with Novo Nordisk in Denmark. Thomas has been an important part of the Malaghan Institute's growth and development these past 12 years and he will be sorely missed. Furthermore, his contribution to the New Zealand biomedical research scene and MS research in particular has been enormous. However, in his future role as head of human T cell biology at Novo Nordisk we will have a good international colleague and collaborator. On behalf of all staff I wish him well. From 2009, Dr Anne La Flamme, a senior immunologist from Victoria University will oversee our MS research programme.

Several of our scientists were recognised with awards this year. Particular highlights include Dr Jacquie Harper and Prof Mike Berridge, who were amongst a team of marine and cell biologists and chemists from around New Zealand to receive the Arthur E Schwarting Award for best paper published in the international Journal of Natural Products in 2007. I was honoured to be the recipient of the prestigious

DIRECTOR'S REPORT

international Pillar of Immunology award for research that I published back in 1990 on Interleukin-4, one of the most influential proteins of the immune system. The cutting-edge research of the Infectious Diseases, Immunoglycomics and Cancer Immunotherapy Groups was also rewarded with Dr Kirman, Dr Stocker and Prof Ronchese respectively having good success in securing funding for their ongoing research programmes. When it comes to stand out performances in 2008, a person that comes to mind is PhD student Dianne Sika-Paotonu. Over the past 12 months she has received incredible accolades for her research into the development of designer vaccines for the treatment of cancer that include winning the Advancing Human Health and Wellbeing category of the 2008 MacDiarmid Young Scientist of the Year Awards, the 2008 Colmar Brunton New Zealand Research Excellence Award, the Australasian Society of Immunology 2008 BD Science Communication Award and the inaugural "Buck Communication Award", at the 2008 NZ ASI meeting. With talented up-and-coming young scientists such as Dianne, the future of New Zealand health research is in very capable hands.

Part of the success of our scientists is due to their access to world-class research facilities. An important technology used by scientists at the Malaghan Institute is the technique of Flow Cytometry. This revolutionary technology underpins all of our research groups and its activities are spearheaded by our hard-working Flow Cytometry Suite Manager, Kylie Price. The Malaghan Institute now houses the most state-of-the-art flow cytometry suite in New Zealand, which was augmented earlier this year by funding from the Maurice Wilkins Centre to purchase the latest in cutting-edge flow cytometry technology, an LSRII benchtop flow cytometer. The LSRII is capable of detecting up to 18 different colours and two physical characteristics, providing our researchers with significantly more freedom with respect to experimental design. The LSRII is a Special Order Research Product (SORP) from Becton Dickinson, and with five lasers instead of the standard three lasers, it is one of only five in the world.

With respect to leading-edge infrastructure, it is important to acknowledge Victoria University of Wellington and the very positive and important role it played in 2008 in stimulating novel science research areas at the Malaghan Institute. The University has invested in new chemistry laboratories located adjacent to the Institute and has begun the development of an exciting new science centre on the Kelburn campus to be finished in 2010, which will create novel opportunities for new forms of biomedical research.

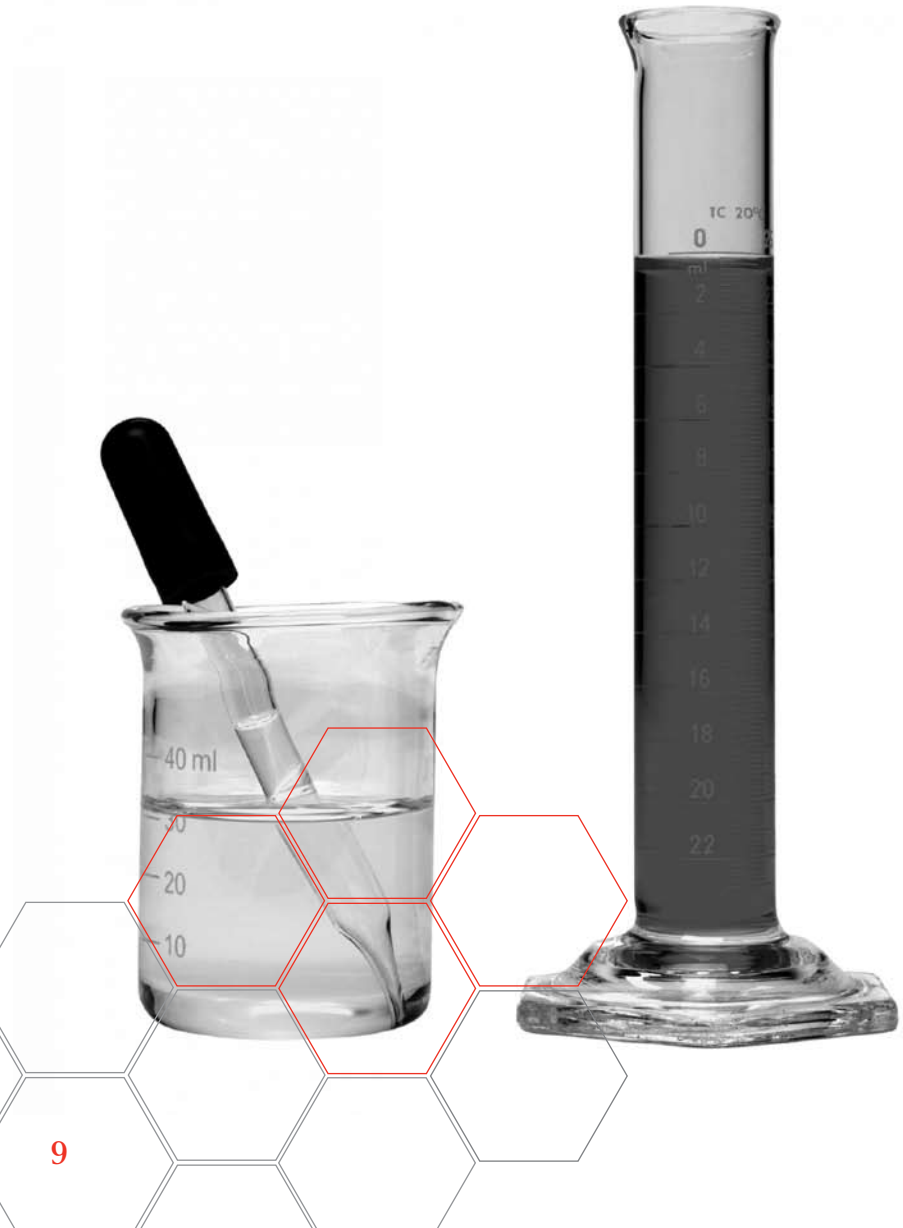
This year the Management structure of the Institute changed with the appointment of Mike Zablocki as Chief Operating Officer. Since then Mike has been actively engaged in defining his role within the Institute and building strategic relationships at the same time as dealing with many infrastructure challenges. These included the design of a new Cell Therapy Centre on Level 1, the establishment of improved building management such as power saving measures, new systems to help manage our repairs, maintenance and assets, as well as on-call staff for building emergencies, significantly upgraded security systems and improved IT infrastructure. I feel very fortunate to have such dedicated and competent staff as Mike and the collective Operations/IT, Finance, Fundraising and Administrative teams working away in the background to ensure the smooth running of the Institute.

The Malaghan Institute Trust Board has continued their very active and valued involvement in the strategic development of the Institute in 2008. In particular I would like to recognise the initiatives of Bryan Johnson, which have resulted in the commitment of financial support by an anonymous US benefactor, allowing the next phase of our cancer vaccine development to be undertaken. This programme is also supported by a generous donation from the Keith Taylor Charitable Trust, which has provided much of the equipment needed for this research. This year a strategic review of the Malaghan Institute was undertaken, which focused on improving staff cohesion, science leadership and science outputs, and the development of an expansive and competitive fundraising strategy to better secure our future in a time of projected economic downturn. Now more so than ever before we rely on the ongoing support of our loyal donors to continue towards our goal of a disease-free future for all New Zealanders.

I would like to finish by expressing my sincerest gratitude to the tireless efforts of our devoted Friends groups and volunteers, to the generous financial support of our corporate sponsors, and to our research collaborators for their significant contributions to our various research endeavours. With such overwhelming support we are well placed to withstand these turbulent economic times and maintain our standing as New Zealand's premier vaccine and immunology research centre.

Prof Graham Le Gros

DIRECTOR



The Malaghan Institute Trust Board plays a critical role in ensuring the future success of our world-class research programmes.

Mr Graham Malaghan *FCILT (Chairman)*

In 1990, was appointed as the Chairman of the Malaghan Institute. He 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. Current directorships include several private companies.

Mr John Beattie *LLB(VUW)*

Obtained a law degree from Victoria University and is a Fulbright Scholar from Cornell University (1979). Has been a Trustee of the Malaghan Institute since 1988 and is Director of Malcorp Biodiscoveries Limited, a subsidiary of the Malaghan Institute. He is also Chairman of the NZ Diabetes Foundation, NZ Sports Hall of Fame and the Wanaka Festival of Colour, is a trustee for the Mt Aspiring College Foundation and the Life Education Trust, and an Executive Director of the Infinity Investment Group.

Prof David Bibby *DSc(Loughborough)*

Was appointed to the Malaghan Institute Trust Board in December 2004. He 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. He holds a PhD in nuclear chemistry and was awarded a DSc in 1995 for his research into zeolites and catysis. He 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

THE MALAGHAN INSTITUTE TRUST BOARD

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 the New Zealand Blood Service, and is currently Medical Leader of the Wellington Cancer Centre and the Chairman of Scots College.

Prof Peter Crampton *MBChB(Otago), PhD(Otago), FAFPHM, MRNZCGP*

Appointed to the Malaghan Institute Trust Board in 2008. Is the current Dean and Head of Campus at the University of Otago, Wellington. 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)*

Obtained a commerce degree from Victoria University 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(Auck), PhD(Auck), FRSNZ*

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. He is a Professor of the Department of Biological Sciences, Victoria University, and has been elected as a Fellow of the Royal Society of New Zealand.

Mr Matthew Malaghan *BCom, MCIT*

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. Returned to New Zealand in 1999. Owns and operates property and mineral processing businesses in New Zealand and Australia. Member of the Charted Institute of Logistics and the NZ Institute of Directors.

Mr David H Mossman *BVSc, MRCVS, MNZIF*

Graduated from the University of Queensland in 1965 with a Veterinary Degree. Awarded the Australian College of Veterinary Scientists college prize in 1978, and the Coopers NZ Farm Management Award for significant innovative farm management concepts of great relevance to pastoral farming in New Zealand in 1984. A major involvement in Beef Cattle production research and delivered Scientific Papers to the New Zealand, Australian, and British Veterinary Associations, and Key note speaker at the World Angus and Hereford Conferences. A Member of the Lindisfarne College Board 1981-85. Managing Director of Farming, Forestry, Finance and Property Development 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*

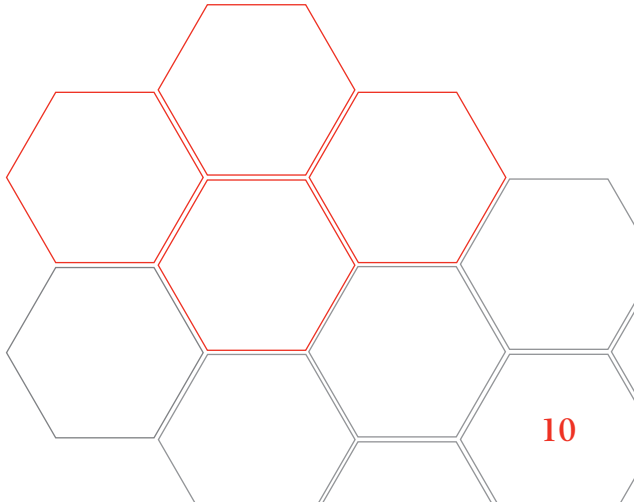
Was appointed to the Malaghan Institute Trust Board in 2001, when he was Managing Director of P&O Nedlloyd in New Zealand. Has an extensive background in the commercial sector both in New Zealand and overseas and is a member of the Institute of Chartered Accountants and Fellow of the Chartered Institute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

Dr Jim Watson *PhD(Auckland)*

Was appointed to the Malaghan Institute Trust Board in 1993. Until recently has been the Chief Executive of Genesis Research & Development Corporation Limited, a company he co-founded in 1994. Has held Professorships at the University of California, Irvine (1976-81) and the University of Auckland (1981-93) serving as Head of the Department of Molecular Medicine (1983-93). He 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 Managing Director of BioJoule Limited, a renewable Energy Company.

Mr C Dan Williams *CA*

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.



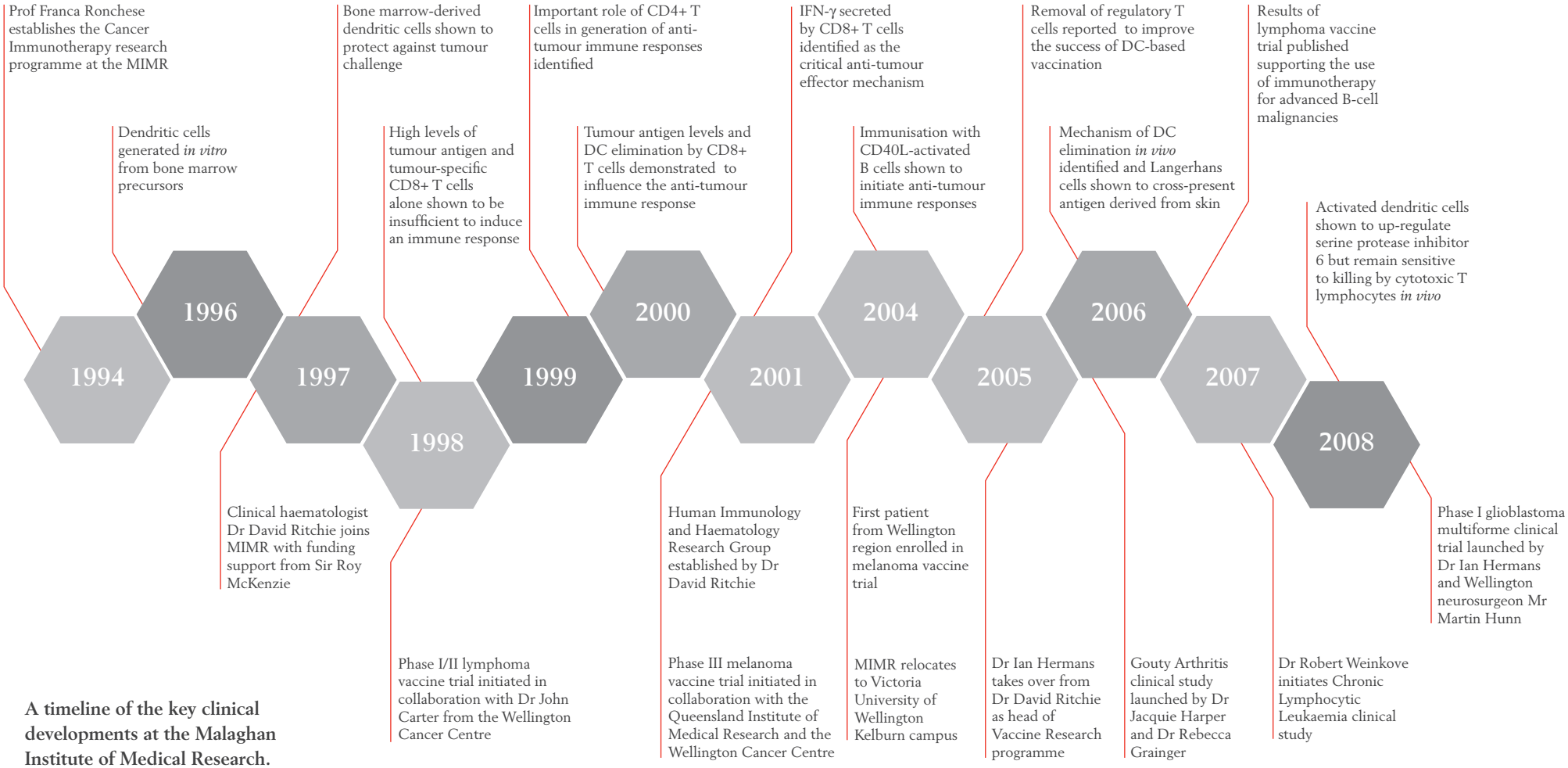
BENCH TO BEDSIDE

Scientists at the Malaghan Institute are leading the charge in the search for more effective ways to exploit the potency and specificity of the immune system by using vaccination to treat diseases such as cancer.

Over the past decade the Malaghan Institute has become increasingly focused on translating our basic biomedical research into real results for patients - a "bench to bedside" philosophy that underpins all our research programmes.

BENCH

BEDSIDE



A timeline of the key clinical developments at the Malaghan Institute of Medical Research.

CURRENT CLINICAL PROGRAMMES

Phase I Glioblastoma Multiforme Clinical Trial

In late 2008 the Malaghan Institute initiated a Phase I clinical trial to test the feasibility and safety of using dendritic cell vaccines in combination with standard chemotherapy for the treatment of patients with recurrent glioblastoma multiforme, a highly aggressive brain cancer with a 100 % fatality rate.

The brain cancer trial is the culmination of over a decade of basic cancer immunotherapy research at the Malaghan Institute and is being overseen by the Head of the Institute's Vaccine Research Group, Dr Ian Hermans, in collaboration with Wellington Hospital neurosurgeon Mr Martin Hunn.

It is anticipated that the trial will involve 12-17 patients from the greater Wellington region that meet a strict set of eligibility criteria. The vaccine will be generated from dendritic cells isolated from the patient's blood that are loaded with pieces of their surgically-removed tumour.

The patients will initially receive three vaccine treatments at two-week intervals, before being given the chemotherapy drug temozolomide. Once chemotherapy has been started, the vaccines will then be given to the patients monthly for up to six months.

Chronic Lymphocytic Leukaemia (CLL) Clinical Study

In December 2007 Malaghan Institute Clinical Research Fellow Dr Robert Weinkove launched a new clinical study into chronic lymphocytic leukaemia or CLL, the most common blood cancer in New Zealand.

The goal of this study is to examine the potential of using a patients own immune system to fight their leukaemia. Working in conjunction with the Wellington Blood and Cancer Centre, and Dr Ian Hermans and Prof Franca Ronchese from the Malaghan Institute, Dr Weinkove is comparing the immune systems of patients with CLL with those of healthy volunteers.

The focus of this study is a rare type of blood cell called the natural killer T (NKT) cells, which are capable of directing the body's immune system. Dr Weinkove believes that NKT cells could be used to improve responses to cancer vaccination, and help 'train' the immune system to recognise leukaemic cells as foreign. This research complements the dendritic cell cancer vaccination programme at the Malaghan Institute.

If the results of this study prove promising, Dr Weinkove will use this translational research to develop future clinical trials of immunotherapy for CLL and other cancers.

Gouty Arthritis Clinical Study

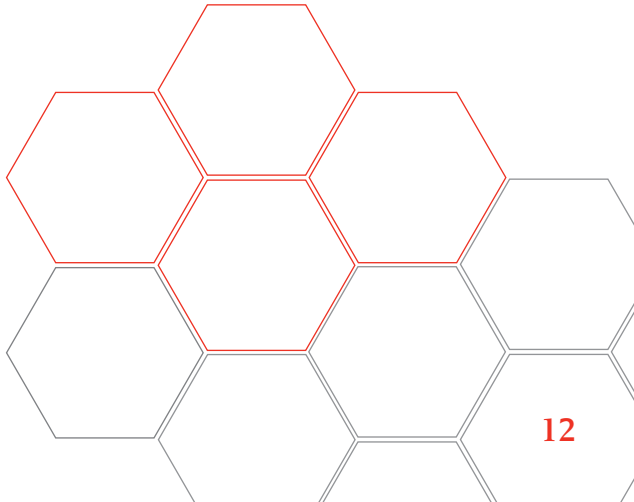
Gout is an extremely painful recurring arthritic disease affecting a great number of New Zealanders, and is the main focus of the Malaghan Institute Arthritis Research Group, led by Dr Jacquie Harper.

The inflammatory response in gout is triggered by the formation of uric acid (MSU) crystals in and around the joints.

In 2006 the Arthritis Group's basic research protocols were successfully translated into a clinical setting with the support of Rheumatologist Dr Rebecca Grainger.

The main objective of the Gouty Arthritis clinical study was to determine whether immune cells isolated from gout patients produced more inflammatory molecules compared with healthy subjects when exposed to MSU crystals.

The study, which is now in the final stages of data analysis, is likely to provide important information on why some individuals are more prone to developing gout than others, and will facilitate the development of preventative strategies for improved management of this disease.



CANCER IMMUNOTHERAPY

Group Members:
Joel Zhi-Iong Ma
Evelyn Spittle
Dr Robert Weinkove
Dr Rachel Perret (to Dec)
Dr Jianping Yang
Haley Ataera
Helen Simkins
Prof Franca Ronchese

Absent from photo:
Dr Noriyuki Enomoto
Jim Qin (to Jan)
Antonia Richter
(Aug to Oct)

Overview

Cancer affects one in three New Zealanders, yet effective cures by conventional treatments remain rare for major cancer types.

Immunotherapy is a promising novel therapeutic approach for many different cancers that has the potential to provide long-lasting protection against relapse.

We are using dendritic cells as the basis of cancer vaccines designed to instruct the immune system to selectively recognise and destroy cancer cells.

We believe that a greater understanding of the basic biology of dendritic cells and how they initiate anti-tumour immune responses will help facilitate their use in cancer immunotherapy.

2008 Research Highlights

Identification of tumour-specific T cell populations that are long-lived and maintain the ability to reject tumours for extended periods of time.

We studied the survival of dendritic cells loaded with different types of antigen during primary and secondary immune responses. We found that the induced immune response may have profound effects on the survival of those dendritic cells.

The phenotype and function of dendritic cells in tumours, and how they might be affected by other cell populations that are also found infiltrating the tumours were determined.

We have started to dissect the mechanisms by which activated CD8+ T cells protect against allergic lung inflammation.

Awards

ASI International Travel Award (HS)

British Society for Haematology Travelling Scholarship (RW)

New Zealand Science & Technology Postdoctoral Fellowship (RP)

Victoria University of Wellington PhD Submission Scholarship (HS)

Funding Sources

Cancer Society of New Zealand
Genesis Oncology Trust
Harry & Beverly Romanes
Health Research Council of New Zealand
Infinity Foundation Ltd
New Zealand Lottery Health Research
The Royal Society of New Zealand
Marsden Fund
University of Otago
Victoria University of Wellington
Wellington Medical Research Foundation

Collaborators

Prof Bill Denny, Auckland Cancer Society Research Centre, The University of Auckland, New Zealand

Dr Michelle Epstein, University of Vienna, Austria

Dr Bill Jordan, Dr Pisana Rawson, Dr Lifeng Peng, Centre for Biodiscovery, Victoria University of Wellington, New Zealand

Collaborators Cont.

Dr Bronwyn Kivell, Victoria University of Wellington, New Zealand

Prof Bernard Malissen, Centre d' Immunologie Marseille-Luminy, France

Prof Niki Romani, Innsbruck University, Austria

Prof Joe Trapani, Peter MacCallum Cancer Centre, Melbourne, Australia

Project One: Regulation of the Immune Response by Perforin

One of the major obstacles to cancer immunotherapy is overcoming the mechanisms that limit current anti-tumour immune responses. We have observed that elimination of dendritic cells by perforin, a protein produced and released by cytotoxic T lymphocytes (CTLs), prevents them from restimulating anti-tumour immune responses.

Early results indicate that while normal CTLs expand little after dendritic cell immunisation, do not increase their ability to secrete cytokines and inhibit the proliferation of other naïve CD4+ and CD8+ T cells, the opposite is true for CTLs that cannot make perforin. This suggests that perforin plays an important role in regulating the outcome of immune responses.

Recently we have shown that the sensitivity of dendritic cells to killing is dependent on how they are loaded with antigen. We are now looking to see if we can take advantage of this information to improve current dendritic cell vaccine design.

We have also launched a new project to investigate how activated CD8+ T cells can inhibit allergic airway inflammation and the role perforin-dependent killing may play in this pathway(s).

Project Two: Intratumoural Antigen Presenting Cells

We are characterising the phenotype and function of immune cells present within unmanipulated tumours. Interestingly, although dendritic cells isolated from tumours were shown to be functional in antigen uptake, they did not activate tumour-specific CD4+ and CD8+ T cells *in vitro*.

We have now extended this study by demonstrating that the inability of the tumour-infiltrating dendritic cells to activate T cells does not appear to be due to the presence of high numbers of suppressive T regulatory cells in the tumours, because depletion of the T regulatory cells did not reverse this effect.

Project Three: Chronic Lymphocytic Leukaemia (CLL) Clinical Study

In December 2007 Haematologist Dr Robert Weinkove launched the Malaghan Institute's first clinical study into CLL, the most common blood cancer in New Zealand. Working in conjunction with the Wellington Blood and Cancer Centre, and Dr Ian Hermans, Dr Weinkove will compare the immune systems of patients with CLL with those of healthy volunteers. The focus of this study is a rare type of blood cell called the natural killer T (NKT) cell, which Dr Weinkove believes could be used to improve responses to cancer vaccination.

Project Four: Survival of Dendritic Cell Subpopulations after αGalCer Administration

Presentation of αGalCer, which is used in dendritic cell vaccines to enhance the anti-tumour immune response, leads to the activation of natural killer T (NKT) cells. We wished to determine whether NKT cells can kill dendritic cells after vaccination and found that αGalCer administration stimulates the disappearance of a subpopulation of spleen dendritic cells. The mechanism of dendritic cell disappearance did not involve perforin but instead appears to be partly mediated by the cytokine TNFα. The significance of this discovery with respect to vaccine design is currently being investigated.

Project Five: Memory T cells in Cancer Immunotherapy

We have characterised populations of tumour-specific T cells that are long-lived yet still effective at fighting tumours. We are currently attempting to define the conditions required to generate these cells in culture. We are also collaborating with proteomic specialists from Victoria University's Centre for Biodiscovery to examine the proteins expressed by these cells. It is anticipated that this information will be highly beneficial for the generation of more effective tumour specific T cells and vaccines.

Professor Franca Ronchese (Group Leader)

Prof Ronchese completed her studies at the University of Padova, Italy, and spent four years as a post-doctoral researcher at the NIH, USA. She then worked as an independent Scientific Member at the Basel Institute for Immunology, Switzerland, before being awarded a Malaghan Senior Research Fellowship. With support from the Wellington Medical Research Foundation, Prof Ronchese established the Cancer Immunotherapy group at the Malaghan Institute in 1994. Prof Ronchese's research centres on the dendritic cell, with a particular focus on the involvement of these cells in the early phases of an immune response, and how dendritic cells can be used to best advantage as carriers in cancer vaccines.

VACCINE RESEARCH

Group Members:

Dianne Sika-Paotonu
Deborah Knight
Dr Peter Ferguson
Dr Ian Hermans
Dr Troels Petersen
Kathryn Farrand
Evelyn Bauer

Absent from photo:
Nina Dickgreber
Dr Scott Harding
Brigitta Mester
Dr Anil Ranchord
Catherine Wood

Overview

T cells with specificity for cancerous tissues need to be activated by specialised immune cells called dendritic cells in order to proliferate and migrate to the target tissue.

Natural killer T (NKT) cells are an excellent source of the signals required for optimal activation of dendritic cells and can thus influence anti-tumour T cell responses.

The overall aim of the Vaccine Research Group is to improve T cell responses by exploiting the activity of NKT cells in the design of more effective vaccines against diseases such as cancer.

2008 Research Highlights

The launch of a phase I clinical trial of dendritic cell-based vaccines in patients with the aggressive brain tumour glioblastoma multiforme.

Publication of our leading-edge research, "Targeting antigen to MHC class II molecules promotes cross-presentation and enhances immunotherapy" in the Journal of Immunology.

We highlighted the importance of targeting resident dendritic cells in our vaccination strategies.

We demonstrated that the effectiveness of our dendritic cell vaccine in eliciting cancer-killing T cells is boosted by stimulating NKT cells with the marine sponge-derived lipid compound αGalCer.

We made significant progress in defining the different functional properties of discrete sub-groups of NKT cells.

Awards

Winner of the Advancing Human Health & Wellbeing category of the 2008 MacDiarmid NZ Young Scientist of the Year Awards (DS-P)

Awards Cont.

Australasian Society of Immunology 2008 BD Science Communication Award (DS-P)

Winner of the inaugural Buck Communication Award, at the 2008 NZ ASI meeting (DS-P)

2008 Colmar Brunton New Zealand Research Excellence Award (DS-P)

Winner of the Wellington Health & Biomedical Research Society PhD communication award (ND)

Funding Sources

Cancer Society of New Zealand

Cancer Society Wellington Division

Foundation for Research Science & Technology

Health Research Council of New Zealand

New Zealand Lottery Health Research

University of Otago

Collaborators

Assoc Prof Rod Dunbar, SBS, The University of Auckland, New Zealand

Prof Vincenzo Cerundolo, University of Oxford, United Kingdom

Prof John Fraser, SMS, The University of Auckland, New Zealand

Dr Sarah Hook, Department of Pharmacy, University of Otago, Dunedin, New Zealand

Collaborators Cont.

Mr Martin Hunn, Neurosurgeon, Wellington Hospital, New Zealand

Dr Carol Johnson, Dr Catherine Barrow, Dr David Hamilton, Wellington Blood & Cancer Centre, New Zealand

Dr Gavin Painter, Industrial Research Limited (IRL), Wellington, New Zealand

Dr Chris Schmidt, Queensland Institute of Medical Research, Australia

Project One: Improving Vaccines with Compounds that Stimulate NKT Cells

We have shown that we can generate very strong anti-tumour immune responses when our standard dendritic cell vaccine is used in combination with αGalCer (stimulates NKT cells). These results complement our earlier discovery that certain combinations of Toll-like receptor ligands improve dendritic cell activity and will be taken into consideration when formulating our clinical vaccine protocols.

We are collaborating with Prof John Fraser from Auckland University to exploit the potent immune-stimulating activity of superantigens to target tumour antigens to dendritic cells. This is a very effective way of getting the target antigen cross-presented to the T cells that mediate anti-tumour immunity.

It is now clear that the structure of the lipid compounds used to stimulate NKT cells influences the ability of NKT cells to enhance dendritic cell function. We are working with Dr Bridget Stocker and Dr Mattie Timmer, who head the Immunoglycomics research at the Malaghan Institute, to investigate whether novel synthesised glycolipids can be used to optimise NKT cell activity and thus enhance immunity to tumours.

Project Two: Increasing the Potency of Dendritic Cell-based Vaccines for the Treatment of Cancer

One of the main aims of our basic research programme is to increase the potency and efficacy of dendritic cell-based vaccines so that we can stimulate strong, long-lasting anti-tumour immune responses.

In 2008 we made the remarkable discovery that when we injected our dendritic cell-based vaccines, a part of the resulting anti-tumour immune response was stimulated by dendritic cells that were already resident in the host. These resident cells appear to acquire tumour antigens from the injected cells, although the mechanism is unknown. We are currently exploring ways to best exploit the activity of the resident dendritic cells in order to get the maximal anti-tumour immune response from our cancer vaccine.

In other work we have been attempting to define the function of different subpopulations of NKT cells to determine which cells we should be targeting in our cancer vaccine protocols. We have shown that a subpopulation of NKT cells containing the CD4 proteins produces a significant quantity of IL-4 *in vivo*, a factor which may influence the development of Th2-driven diseases such as asthma. This work is currently being prepared for publication.

Project Three: Using Dendritic Cell-based Vaccines in the Clinic

In 2008 we completed our protocol validation studies into the development of dendritic cell-based vaccines for the treatment of glioblastoma multiforme (brain cancer) and hope to treat our first patient in January 2009. It is anticipated that this phase I clinical trial will involve 12-17 patients from the greater Wellington region that meet a strict set of eligibility criteria.

The goal of this study is to determine if vaccination works better when combined with chemotherapy.

Personalised vaccines such as those being used in the brain cancer trial are very intensive to produce, but they do offer a broad immunity that recognises the unique features of an individual patient's tumour tissue. Realistically, well-defined vaccine targets are needed if we are to take vaccination into much larger clinical trials. We therefore intend to work backwards from any patients that show a positive response to the personalised dendritic cell-based vaccine treatment to identify the most effective antigenic targets on their tumour cells. Defined targets that are common to many patients could then be used to develop simpler vaccines with more wide-spread application.

Dr Ian Hermans (Group Leader)

Overseeing the Malaghan Institute's current involvement in cancer vaccine clinical trials is Dr Ian Hermans, Head of the Vaccine Research group. Dr Hermans studied dendritic cell-based vaccination with Prof Ronchese at the Malaghan Institute between 1995 and 2001, before taking up a position at the Tumour Immunology Unit, Weatherall Institute of Molecular Medicine, at the University of Oxford, UK. In 2005 Dr Hermans returned to the Malaghan Institute and was awarded a Sir Charles Hercus Research Fellowship from the Health Research Council of New Zealand to pursue his research into improving the potency and efficacy of vaccines by exploiting the activity of NKT cells. His group has shown that NKT cells have the capacity to directly enhance the function of dendritic cells, and thus indirectly influence the quality of the whole immune response.

CANCER CELL AND MOLECULAR BIOLOGY

Group Members:

Kate Broadley
Dr Melanie McConnell
Prof Mike Berridge
Carole Grasso
An Tan

Absent from photo:
Taryn Osmond

Overview

The focus of most anticancer drug treatments is on killing the rapidly-dividing cells that form the bulk of a tumour. However, these treatments do not get rid of the 'cancer stem cells' that give rise to the disease and are drug and radiation resistant, so the tumour is able to grow back.

We have identified and characterised a plasma membrane electron transport pathway (PMET) that is essential for cancer cell proliferation and may be required for the survival of cancer stem cells that employ glycolytic metabolism.

Our research aims to understand the role of PMET in cancer stem cell survival and self-renewal, and to develop drugs that compromise this energy support system. We are also evaluating the potential of using immunotherapy to target cancer stem cells.

2008 Research Highlights

We have initiated a collaborative Melanoma Research Alliance Cancer Stem Cell Immunotherapy Programme with the Ludwig Institute.

Human melanoma cell cultures have been established.

Primary spheroid lines were successfully grown from glioblastoma multiforme patients and shown to contain self-renewing cancer stem cells.

We further elucidated the mechanism of action of Novogen's anticancer drug phenoxodiol.

Novel membrane-active lipophilic cations were synthesised and shown to strongly inhibit proliferation of human leukaemic cells.

Awards

Arthur E Schwarting Award for best paper published in the Journal of Natural Products in 2007 (MB)

Collaborators

Prof Aldo Andreani, Prof Laura Landi & Dr Cecilia Prata, University of Bologna, Italy

Dr David Brown, Novogen Inc, Sydney University, Australia

Prof Jonathan Cebon, Ludwig Institute, Melbourne, Australia

Prof Alison Downard, Chemistry Dept, University of Canterbury, New Zealand

Collaborators Cont.

Dr Patries Herst, Department of Radiation Therapy, University of Otago, New Zealand

Dr David Ritchie, Peter MacCallum Cancer Institute, Melbourne, Australia

Prof Robin Smith, Chemistry Dept, and Dr Lesley Larsen, Crop & Food Research, University of Otago, New Zealand

Funding Sources

Cancer Society of New Zealand

Genesis Oncology Trust

Marshall Edwards Inc

Melanoma Research Alliance

Morris Cancer Research Foundation Trust

Roy McKenzie

The Royal Society of NZ Marsden Fund

Project One: The Cancer Stem Cell as a Target for Cancer Treatment

Like the stem cells that shape the development, repair and replacement of various tissues and organs in our body, cancer stem cells or tumour-initiating cells also self-renew and differentiate into other tumour cell types, and can divide indefinitely.

We are attempting to model the glioblastoma multiforme (GBM) cancer stem cell. GBM is the most common brain cancer and patients with the disease have a very poor prognosis.

The goal of this research is to establish cell lines that mimic the complex nature of GBM stem cells and can be used to screen for compounds that compromise their survival. We also plan to use cancer stem cells isolated from immortalised cell lines and GBM tumours as antigen sources for the generation of cancer vaccines. This is being undertaken in collaboration with Dr Ian Hermans and Wellington Hospital neurosurgeon Mr Martin Hunn.

We have shown that we can generate neurospheres from tumour cell lines and glioblastoma tissue and that these spheres contain stem cell-like cells that can form tumours in immunocompromised mice.

Molecular profiling of these spheres has revealed a significant elevation of self-renewal genes relative to serum-grown cells that do not form spheres, supporting the presence of cancer stem cells in neurospheres.

Project Two: Immunotherapeutic Targeting of Melanoma Stem Cells

In July 2008, a global collaborative Melanoma Research Alliance programme was initiated by Prof Jonathan Cebon, Ludwig Institute, Melbourne with the aim of defining melanoma stem cell markers that will be useful for vaccination or immunotherapy.

For several years now, we have been developing cancer stem cell models for drug targeting and were one of the first groups in the world to show the presence of germ cell markers on stem cells. This collaborative research programme builds on the observations that the germ cell markers called CT antigens re-emerge in a small number of melanoma cells, and that these markers can be targeted by the patient's own immune system resulting in tumour-free survival.

Because very few melanoma cells express these antigens, the results suggest that melanoma is populated by a small population of rogue 'stem cells'.

Although still in the early stages of this project, human melanoma cell lines have now been established and the stem cell marker, CD133, used to sort and subsequently culture cells. We are also establishing tumour growth and serial passage in immunocompromised NOD/SCID mice to investigate the stem cell properties of these cells.

Project Three: Drug Targets on Tumour Cells & Immune Cells

One of the main objectives of this research is to develop novel anti-cancer drugs that interfere with PMET. In collaboration with Prof Rob Smith, we have designed and tested more than 20 compounds, with lipophilic cations being the most potent inhibitors of PMET and tumour cell proliferation. A promising drug target of this pathway is the plasma membrane NADH oxidase enzyme. We are currently profiling the various splice variants of this enzyme on tumour cells to establish their drug sensitivity. We are also working with Novogen's anticancer drug phenoxodiol, which is thought to induce apoptosis in cancer cells by blocking the function of a cell surface NADH oxidase. We have shown that while phenoxodiol does inhibit PMET and cancer cell proliferation, it is highly immunosuppressive, suggesting a target molecule is also present on T cells.

Project Four: Acute Responses to Reductive Stress & the Regulation of Gene Expression

SIRT1 is a member of the sirtuin family of NAD+-dependent deacetylases that plays a critical role in regulating a number of intracellular processes in response to changes in NAD+ levels. We have examined the interplay between SIRT1 and PMET in various cancer cell lines following knock-down of SIRT1 expression and have shown that loss of SIRT1 affects the cytotoxicity of PMET inhibitors. This work is currently being prepared for publication.

Professor Mike Berridge (Group Leader)

Prof Berridge completed his postgraduate degree in Cell Biology at the University of Auckland in 1971. Following postdoctoral research at Purdue University, United States of America, and the National Institute for Medical Research, United Kingdom, Prof Berridge returned to Wellington in 1976 as the second Malaghan Fellow. He recently held a James Cook Fellowship in the Health Sciences. Prof Berridge's current research concerns the elusive cancer stem cell, a minor population of quiescent, drug-resistant cancer cells that are thought to be responsible for the initiation of most cancers and their recurrence following treatment. His research group has developed cancer stem cell models for drug targeting and are now investigating immune responses against stem cells. Prof Berridge's research also centres around a stress adaptation and survival pathway in the cell membrane that has particular relevance to tumour cells, which is being targeted with small molecules designed to disrupt the pathway and eradicate cancer.

ARTHRITIS AND INFLAMMATION

Group Members:

Neal Kerr
Dr Mischa Walton
Tommy Liu
Dr Rebecca Grainger
Aras Toker
Dr Jacquie Harper
Willy-John Martin
Clare Slaney
Henry Hudson

Absent from photo:
Stefanie Steiger

Overview

Gout is an extremely painful recurring arthritic disease that is caused by the build-up of uric acid crystals (MSU) in the joints.

In New Zealand the prevalence of gout is twice that observed internationally and it is three times more common in Māori and Pacific Island populations.

The main objective of our research is to identify the factors involved in the onset, duration and resolution of inflammation during attacks of gouty arthritis. This will lead to the development of new treatments for the underlying cause(s) of the disease, including ways to identify susceptibility to inflammation in arthritis sufferers.

2008 Research Highlights

We demonstrated the efficacy of using low-dose colchicine to treat gout, which has the advantage of lower side-effects. The results of this work were published in the British Journal of Pharmacology.

Our gout clinical study revealed that immune cells from patients with hyperuricaemia and/or gout produce higher levels of inflammatory molecules, compared to healthy subjects, when exposed to the gout causing agent MSU crystals. This finding indicates sensitivity to MSU crystal stimulation in these individuals.

We published our findings on monocyte involvement in gout in Arthritis & Rheumatism (the leading Journal for the field of Rheumatology and Arthritis).

Awards

Arthur E Schwarting Award for best paper published in the Journal of Natural Products in 2007 (JH)

Clinical Science Research PhD Prize, Otago University (RG)

Nga Kete a Rehua National Māori Research Symposium, Co-equal prize for best post-graduate talk (W-JM)

Awards Cont.

Nga Pae o te Maramatanga Doctoral Bridging Grant (W-JM)

2008 NZ ASI Meeting Student Speaker Competition, third prize (W-JM)

Toihuarewa Travel Grant, Te Kawa a Māori, VUW (W-JM)

Tom Highton Award for Best Research Talk at the 2008 NZ Rheumatology Conference (JH)

Funding Sources

Arthritis New Zealand

Foundation for Research, Science & Technology

Health Research Council of New Zealand

New Zealand Lottery Health Research

Nikau Foundation (previously Wellington Region Foundation)

Wellington Medical Research Foundation

Collaborators

Assoc Prof Brent Copp, The University of Auckland, New Zealand

Prof Carolyn Geczy, University of New South Wales, Sydney, Australia

Dr Andrew Harrison, University of Otago - Wellington School of Medicine, New Zealand

Dr Roger Hurst, HortResearch Ruakura, Hamilton, New Zealand

Collaborators Cont.

Dr Stephen Geiseg, University of Canterbury, New Zealand

Dr Keryn Johnson, Industrial Research Limited, Lower Hutt, New Zealand

Dr Nigel Perry, Crop and Food Research, New Zealand

Dr Vicky Webb, NIWA, New Zealand

Dr Antony Wheatley, University of Otago, New Zealand

ARTHRITIS AND INFLAMMATION

Project One: Role of Macrophages and Monocytes in Acute Gouty Arthritis

Recruitment of immune cells called monocytes to the joints and connective tissues is a key characteristic of the inflammatory response observed in a variety of arthritic diseases.

In 2008 we published our pivotal finding that the resident macrophage is the key cell responsible for producing the initial inflammatory response to MSU, including the recruitment of damage-causing neutrophils that exacerbate the disease. In contrast, monocytes entering the site of inflammation contribute little to the initiation and early progression of inflammation induced by MSU crystals.

We are continuing to investigate the infiltrating monocyte populations in gouty arthritis to determine how their presence at the site of inflammation might be contributing to disease progression.

In other work we showed that the drug colchicine suppresses MSU-induced superoxide production by neutrophils in a murine model of gouty arthritis at sub-toxic doses. This is the first *in vivo* data to provide compelling support for the use of low dose, non-toxic, colchicine therapy for the treatment of gouty arthritis.

Project Two: A Clinical Study of Gouty Arthritis

Elevated levels of uric acid in the blood (hyperuricaemia) are a prerequisite for gout, however only 20% of individuals with hyperuricaemia go on to develop gout and it is unclear why the other 80% remain asymptomatic.

Three years ago we launched a clinical study to investigate whether immune cells isolated from patients with hyperuricaemia and/or gout, produce more inflammatory molecules compared with healthy subjects when exposed to the gout causing agent MSU crystals.

Our study has revealed significant differences in sensitivity to MSU crystal stimulation in gout patients compared with healthy individuals that might serve as a prognostic marker for developing the disease.

We are now in the final stages of data analysis and hope to publish the findings of this study in 2009.

Project Three: New Anti-inflammatory Treatments for Arthritis

In 2008 our anti-inflammatory research was recognised with the award of the prestigious Arthur E Schwarting Award for best paper published in the international Journal of Natural Products last year. The paper describes the discovery of two novel natural compounds from a sea squirt found in New Zealand's coastal waters that can inhibit acute inflammation.

This work represents the culmination of a joint venture, TerraMarine Pharmaceuticals, that was formed in 2002 between the Malaghan Institute, Crop and Food Research, The University of Auckland and the National Institute of Water and Atmospheric Research, to screen New Zealand's unique plant and marine life for novel bioactive compounds.

This work is underpinned by a patent application around the structure and application of these compounds for the treatment of arthritis and other inflammatory diseases involving neutrophils.

We are also involved in an ongoing collaboration with HortResearch to develop anti-inflammatory neutraceuticals for improving the management of inflammatory conditions.

Dr Jacquie Harper (Group Leader)

Dr Harper obtained her PhD in Chemistry and Physiology from the University of Otago. After a Post-doctoral position with the Physiology Department at the University of Otago, Dr Harper took up a Fogarty Research Fellowship at the National Institutes of Health (United States of America) in the Laboratory of Biological Chemistry. As Head of the Arthritis & Inflammation Group, Dr Harper's main research interests lie in the role of innate immune cells in driving arthritic diseases and the development of novel anti-inflammatory treatments for improved disease management.

IMMUNOGLYCOMICS

Group Members:

Dr Ben Mulchin
Emma Dangerfield
Catherine Plunkett
Dr Bridget Stocker
Ashna Khan
Dr Mattie Timmer
Janice Cheng
Anna Win
Gregory Haslett
Dr Lynton Baird

Overview

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

In 2007 we established an Immunoglycomics research initiative between the Malaghan Institute and Victoria University of Wellington (VUW). Through the synthesis of complex glycans, the Immunoglycomics programme focuses on understanding the role of carbohydrates in the immune response and has several areas of disease focus including asthma, cancer and tuberculosis.

2008 Research Highlights

In 2008 we developed new methodology that enables designer drugs to be synthesised more efficiently and in a way that is better for the environment ("green chemistry"). This cutting-edge discovery has led to a publication and a provisional patent application.

We are currently using this methodology to develop therapeutics targeted against Tuberculosis, but also plan to apply this approach to other diseases in the near future.

In 2008 we synthesised several novel compounds to test in high throughput assays for their ability to treat cancer, inflammation or asthma. Some of our anti-cancer compounds have already shown promising activity.

Awards

Tertiary Education Commission Top Achiever Doctoral Fellowship (ED)

Tertiary Education Commission Masters Fellowship (AW)

Tetrahedron Asymmetry – most cited paper 2005 – 2008 (MT)

Vice Chancellor PhD Scholarship, VUW (AK)

Victoria Graduate Award (GH, JC)

Victoria University Equity Grant (JC)

Zonta Science Award (Finalist) (BS)

Collaborators

Industrial Research Ltd, New Zealand

New Zealand Pharmaceuticals

Victoria University of Wellington, New Zealand

Funding Sources

Cancer Society Wellington Division

The Foundation for Research Science & Technology

Health Research Council of New Zealand

New Zealand Lottery Health Research

Sir Roy McKenzie Industrial Research Limited Charitable Trust

Victoria University Research Grant

Wellington Medical Research Foundation

Project One: A Sweet Approach to Asthma

While much is known about the causes of asthma, few studies have looked at the molecular structures of the allergens that trigger the disease and the role they play in influencing Th2 immune responses.

Upon close examination of the structural features of allergens such as pollen, food, and worms, we observed that particular structures (carbohydrates) were conserved. Interestingly, antigens derived from bacteria and viruses neither possess these carbohydrate structures nor stimulate allergic immune responses, leading us to hypothesise that these unique structural motifs might be responsible for biasing the immune response towards Th2.

To investigate this hypothesis we are in the process of synthesising a library of carbohydrates for testing in Th2 immune response assays.

We hope that these studies will provide the first detailed insight into the relationship between carbohydrate structure and Th2 bias and will lead to the identification of specific Th2 targets that will aid in the diagnosis and treatment of asthma and allergy.

Project Two: Small Molecules in Cancer Therapy

A) *Cancer Immunotherapy:* Immunotherapy holds promise as a new treatment for cancer. In a typical cancer immunotherapy programme, tumour cells are extracted from a patient and used to prepare a vaccine designed to stimulate an anti-tumour immune response. Though tumour regression has been observed in a number of patients using this approach, the immune response is not robust. The addition of certain glycolipids however, acting as adjuvants, boosts 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. We are currently synthesising a variety of novel glycolipids to enhance anti-tumour immunity.

B) *Natural Products to Target Cancer:* A number of compounds isolated from natural sources are known to have anti-cancer potential. Our efforts in this area focus on the synthesis of natural product derivatives (quinones), which have been shown to have an interesting mode of action in the killing of tumour cells. On route to synthesising our final quinone targets, we have also identified many other promising lead compounds.

Project Three: Synthesis of Designer Drugs against *Mycobacterium tuberculosis*

Tuberculosis (TB) kills more people than any other infectious disease. A staggering one-third of the world's population is infected with *Mycobacterium tuberculosis*, the causative agent of TB. Though once considered to be a third-world disease, over recent years there has been an increase of tuberculosis in the so-called 'developed countries'. In New Zealand a person contracts tuberculosis daily. The current vaccine for tuberculosis, BCG (Bacillus Camette Guerin), is the least effective vaccine in use today with reports of its efficacy ranging from 0 to 80%. Additionally, drug resistant strains of TB have emerged.

In view of the problems associated with current TB treatments, we aim to synthesise a novel class of drugs that target the sugar-making enzymes involved in maintaining the structural integrity of the mycobacterial cell membrane. Arabinose sugars are crucial to the survival of mycobacteria but are not found in humans, so a drug designed against their synthetic pathway is likely to kill the bacteria while having minimal side-effects on the patients being treated.

These compounds are being synthesised using a novel approach that we developed in 2008, which gives high yields while having the added advantage of being better for the environment.

Dr Bridget Stocker (Group Leader)

Dr Stocker was awarded the Victoria University of Wellington Gold Medal for the top graduating BSc(Hons) student in 2000, and continued on at Victoria University for her PhD, focusing on the total synthesis of several anti-cancer agents. Following a brief period as a lecturer at Victoria University, Dr Stocker was awarded a FRST Bright Futures Post-Doctoral Fellowship in 2004 and spent two years at the prestigious Swiss Federal Institute of Technology, Zurich, where she completed the total synthesis of several complex mycobacterial glycans. In 2006, Dr Stocker returned to New Zealand, and a position at the Malaghan Institute. The Immunoglycomics programme was established in 2007 in collaboration with Victoria University of Wellington (Dr Mattie Timmer, School of Chemical and Physical Sciences).

ASTHMA AND PARASITIC DISEASES

Group Members:

Sarrabeth Stone
Marina Harvie
Dr Elizabeth Forbes
Melanie Prout
Mali Camberis
Shiau-Choot Tang
Prof Graham Le Gros
Helen Mearns

Absent from photo:
Dr Nicholas van Panhuys
(to Apr)

Overview

Despite ongoing research there is currently an epidemic of allergic diseases in the Western world. Asthma is a chronic respiratory allergic disease of major concern to our community, affecting one in four New Zealand children and one in six adults. It is now clear that the final symptoms of asthma are paradoxically due to our body's own immune system overreacting to quite harmless environmental triggers (allergens) such as pollen or house dust mites.

A major focus of our research is to define the basic biology of the Th2 immune response that gives rise to asthma, and the chemistry of the allergens that stimulate this response. We hope to apply this knowledge to the development of generally applicable vaccines and improved therapies for the treatment of individuals with established disease.

2008 Research Highlights

Pioneering research first published by Prof Le Gros in 1990, on which this research programme is built, received a major international honour by being selected as a "Pillar of Immunology".

Using a cutting-edge allergy assay developed by our group we have made significant progress into defining the physical and chemical properties of what makes an allergen an allergen.

Our provocative work demonstrating IL-4 independent Th2 immune responses was published in the Proceedings of the National Academy of Sciences, USA.

Awards

2008 Claude McCarthy Fellowship (MH)

New Zealand Science and Technology Postdoctoral Fellowship (EF)

Pillar of Immunology (GLG)

Collaborators

Dr Volker Brinkmann,
Novartis, Switzerland

Dr Melanie Kleinschek,
SP Biopharma, United States of America

Prof Rick Maizels,
University of Edinburgh,
United Kingdom

Dr Booki Min, Cleveland Clinic,
United States of America

Collaborators Cont.

Dr William Paul, NIAID,
National Institutes of Health,
Washington DC,
United States of America

Prof Neil Pearce & Assoc Prof Jeroen Douwes, Centre for Public Health Research, Massey University, Wellington, New Zealand

Prof Murray Selkirk, Imperial College London, United Kingdom

Funding Sources

AMI Insurance

Foundation for Research, Science & Technology (FRST)

Health Research Council of New Zealand

Marjorie Barclay Trust

New Zealand Lottery Health Research

Rex & Betty Coker Scholarship

The Royal Society of New Zealand Marsden Fund

ASTHMA AND PARASITIC DISEASES

Project One: Modelling Allergy and the Th2 Immune Response

Conventional treatments for allergy and asthma, such as steroids, target the downstream steps of allergic inflammation. However, how the Th2 responses are induced in allergy and why some allergens preferentially promote Th2 responses in only a subset of individuals are still unknown.

To address these questions we have developed a novel assay to look at the early events of Th2 sensitisation in response to allergens known to trigger asthma such as house dust mites, pet dander, cockroaches and nematode worms. We are also working with Prof Richard Beasley to look at the effect of paracetamol on the induction of Th2 immune responses in our allergy model.

In 2008 Dr Elizabeth Forbes received funding to develop an experimental model that is relevant to human exposure through the skin, with a focus on the interrelationship of food allergy with other allergic disease processes. Previous studies have demonstrated that childhood allergic diseases often start in the skin as atopic dermatitis and later progress to the gastrointestinal and respiratory tracts.

The outcome of this research will be the development of scientifically sophisticated and physiologically relevant experimental models of allergy.

Project Two: The Basic Biology of the Th2 Immune Response

Before we can realistically start to provide practical advice on how best to avoid asthma and allergy, a greater knowledge of the basic biology of the Th2 immune response is required. Research published by our group in 2008, clearly illustrated that *in vivo* differentiation of naïve CD4 T cells to Th2 status can occur independently of IL-4 and STAT6 signaling; highlighting an as yet undefined alternative pathway for Th2 differentiation. Our current studies are focused on identifying alternative cytokine candidates and their potential roles in driving an IL-4-independent differentiation of Th2-mediated immunity to allergens and parasitic infection. We are also investigating the key parameters of Th2 protective immunity and the role of lymphocyte recirculation in allergic responses using the drug FTY-720.

Project Three: Parasites and the Th2 Immune Response

Two billion people worldwide are infected with intestinal nematodes such as hookworms, which cause intestinal blood loss, protein malnutrition and anaemia. Using the harmless laboratory-adapted rodent nematode *Nippostrongylus brasiliensis*, which has similarities to human hookworm and provokes immune responses reminiscent of asthma, we have shown that the lung is a central site for inducing protection against re-infection. This information will assist in the development of vaccination strategies against these parasites.

Project Four: What Makes an Allergen, an Allergen?

We are using a multi-disciplinary approach to tackle the intriguing question of what makes an allergen, an allergen. Although much is known about the types of allergens that cause asthma, our knowledge of their molecular structures is very limited.

To define an allergen at the protein level we are extracting natural allergens and developing methods for their isolation and identification such as high performance liquid chromatography (HPLC), 2-Dimensional Gel Electrophoresis and MALDI Mass Spectrometry. These allergenic structures will be validated in our models of Th2 induction.

We are also testing a library of carbohydrate structures synthesised by the Malaghan Institute Immunoglycomics Group in our Th2 immune response assays. These structures were shown to be conserved on allergens such as pollen, food and worms but not present on antigens derived from bacteria and viruses that do not stimulate Th2 immune responses.

These studies will provide the first detailed insight into what makes an allergen at the protein and sugar levels, and will allow us to identify putative therapeutic targets for the treatment of allergic diseases.

Professor Graham Le Gros (Group Leader)

Prof Le Gros was appointed Research Director of the Malaghan Institute in 1994, following a three year Fogarty Fellowship at the National Institutes of Health (NIH), Washington DC, and a five year scientist position with Ciba-Geigy in Basel, Switzerland. He is a member of the Cancer Society's Scientific Committee, Lotteries Health Committee, Wellington Medical Research Foundation Scientific Committee, various science advisory groups and is a Professor of the Department of Biological Sciences, Victoria University. In 2005 Prof Le Gros was elected as a Fellow of the Royal Society of New Zealand in recognition of his research contributions to the fields of immunology and asthma. Prof Le Gros' overall research interest lies in understanding the basic biology of Th2 immune responses, with a particular focus on the mechanisms and cell types involved in mediating allergic and asthmatic inflammation.

INFECTIOUS DISEASES

Group Members:

Lisa Connor
Fenella Rich
Dr Joanna Kirman
Clarissa Chandrahasen

Absent from photo:
Susanna Brow (to Sep)
Kasper Eckert (to Mar)
Hannah Kelly (to Nov)
Dr Kylie Quinn (to Jun)
Victoria Taylor (to Feb)
Catherine Wood (to May)

Overview

Tuberculosis (TB) kills more people worldwide than any other bacterial infection. It is estimated that one New Zealander a day is being newly diagnosed with TB, a rate higher than that in Australia, the USA and Canada. Prevention of TB through the development of an effective vaccine is a global health priority.

Studies of TB and other viruses of particular relevance to New Zealanders, such as the paediatric viruses rotavirus and respiratory syncytial virus, are crucial to determining appropriate vaccine design and administration.

The ultimate goal of our research is to reduce the incidence of infectious disease in New Zealand through the development and implementation of vaccines.

2008 Research Highlights

In 2008 we made significant progress in the development of a more effective TB vaccine by determining the likely location of the immune cells responsible for mediating vaccine-induced protection against the bacteria that cause the disease.

Data collection for a multi-centre rotavirus strain surveillance study was completed.

We also initiated a collaborative pilot study with the Wellington Asthma Research Group to identify possible interventions to RSV-induced hospitalisation.

Awards

Claude McCarthy Fellowship (LC)

Fogarty International Fellowship (USA) (KQ)

NZ ASI Branch Meeting: Runner-up, student oral presentations (LC)

Wellington Medical Research Foundation Travel Scholarship (LC)

Wellington School of Medicine 1st equal award for Best Summer Student Project (VT)

Funding Sources

Health Research Council of New Zealand

Merck, Sharp & Dohme New Zealand

Foundation for Research, Science & Technology (FRST)

New Zealand Lottery Health Research

University of Otago

Victoria University of Wellington

Wellington Medical Research Foundation

Collaborators

Dr Volker Brinkmann, Novartis, Switzerland

Dr Bryce Buddle, Dr Geoff deLisle and Dr Michel Denis, AgResearch, Wellington, New Zealand

Prof Julian Crane and Dr Tristram Ingham, Wellington Asthma Research Group, University of Otago, New Zealand

Collaborators Cont.

Prof Brett Delahunt, Department of Pathology, Wellington School of Medicine, New Zealand

Prof Keith Grimwood, Royal Children's Hospital, Queensland Health, Brisbane, Australia

Dr Shaun Lott, The University of Auckland, New Zealand

Dr Ronan O'Toole, Victoria University of Wellington, New Zealand

Collaborators Cont.

Also New Zealand contributions by:

Aotea Pathology

Capital & Coast Health Laboratory

Health Waikato

Hutt Hospital Laboratory

Medlab South

Paediatric Units and laboratories at Canterbury Health

Starship Auckland Hospital

Southern Community Laboratories

Project One: Tuberculosis (TB) Vaccine Development

The currently available vaccine against Tuberculosis, BCG, has been given to more than three billion people worldwide, yet it fails to consistently provide protection against the bacterium that causes the disease. Efforts to develop a new, more effective vaccine for TB have been hampered by a lack of understanding of what constitutes a protective memory immune response.

We are currently trying to understand which of the protective cell types generated after BCG vaccination are important for mediating vaccine-induced protection against TB. In 2008 we determined the likely location of the protective memory cells against TB using a drug called Fingolimod, which traps cells in the lymph node and are now focused on refining this critical discovery.

In other work, in collaboration with Dr Shaun Lott from The University of Auckland, we are developing vaccines targeted against multiple TB antigens. During an early infection the TB bacterium grows very fast before it enters a dormancy or latency phase in which its growth gradually tapers off. The antigens produced during the fast and dormant growth phases are quite different, so by developing a vaccine that targets both we hope to more effectively halt the progression of this deadly disease.

Project Two: Multicentre Rotavirus Strain Surveillance

Rotavirus is a highly contagious virus that most commonly affects children under the age of two. It causes diarrhoea and vomiting, resulting in approximately 1000 hospitalisations in this country each year. Over the past three years we have been collecting data for a multi-centre rotavirus strain surveillance study aimed at monitoring New Zealand's rotavirus strains pre- and post-introduction of a commercial rotavirus vaccine. This information will be vital for predicting the potential effectiveness of the vaccines that will be introduced into New Zealand.

Early indications from this study have shown a strong geographical link between the different rotavirus strains, with those prevalent in the South Island each winter differing to those prevalent in the North Island. Furthermore, while the predominant strain seen globally and in NZ is consistently G1, the strains making up the remaining 40-50% change quite dramatically each season and no-one knows why.

Two rotavirus vaccines have been recommended for inclusion in the national immunisation schedule but have yet to be approved. If a vaccine is approved, we will aim to re-establish strain surveillance to determine the effect of the introduced vaccine(s) on circulating rotavirus strains.

Project Three: Interventions to RSV-Induced Hospitalisation

Respiratory syncytial virus (RSV) is one of the leading causes of infant hospitalisation, affecting more than 95% of children under the age of two.

We have shown previously that Māori and Pacific infants have a higher risk of being hospitalised from RSV bronchiolitis than NZ European infants.

In 2008 we initiated a collaborative pilot study with the Wellington Asthma Research Group to identify possible interventions to RSV-induced hospitalisation, in an effort to reduce the rate of severe RSV infection in this country.

This study is focused on determining whether vitamin D levels correlate with the ability to protect against RSV infection and hence disease severity.

Samples are currently being collected for analysis in 2009.

Dr Joanna Kirman (Group Leader)

After completing her postgraduate training in infectious disease-based immunology at the University of Otago and the Malaghan Institute, Dr Kirman was awarded a Fogarty Fellowship to pursue her work in vaccine development at the National Institute of Allergy and Infectious Diseases, United States of America. Dr Kirman returned to the Malaghan Institute in July 2002 to lead the Infectious Diseases Group as a Sir Charles Hercus Research Fellow, supported by the Health Research Council of New Zealand.

MULTIPLE SCLEROSIS

Group Members:

Evelyn Spittle (to Sep)
Clare Slaney
Aras Toker
Dr Elizabeth Forbes (to Dec)

Absent from photo:
Assoc Prof Thomas Bäckström (to Aug)

Overview

Multiple Sclerosis (MS) affects one in every 1,100 New Zealanders, and there is no known cure for the disease. It 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.

In a healthy individual, the immune system maintains a balance between triggering an inflammatory response and an equilibrium maintained by cells that regulate it. In MS, this balance is disrupted.

The focus of our research is to better understand the cause(s) of MS and to use this knowledge to develop therapeutic treatments that can be used to halt its progression.

2008 Research Highlights

We progressed our MS immunotherapy research by successfully generating regulatory T cells capable of migrating to sites of inflammation.

We showed that we can inhibit the development of MS in a murine model of the disease using a compound that binds to and enhances the activity of a novel population of suppressor cells.

We gained new insight into how the drug Glatiramer acetate might protect against the development of MS.

Although not a highlight, a significant development in the MS Group in 2008 was the sad departure of Assoc Prof Bäckström to Novo Nordisk in Denmark. From 2009, Dr Anne La Flamme, a senior immunologist from Victoria University will oversee our MS research.

Awards

ASI International Travel Award (AT)

Wellington Medical Research Foundation Travel Scholarship (CB)

Collaborators

Prof Claude Bernard, Monash University, Melbourne, Australia

Prof John Fraser, The University of Auckland, New Zealand

Dr Ian van Driel, University of Melbourne, Australia

Funding Sources

Health Research Council of New Zealand

New Zealand Lottery Health Research

Nikau Foundation (previously Wellington Region Foundation)

Wellington Medical Research Foundation

Project One: Evaluating the Therapeutic Potential of Exploiting Regulatory T Cells to Treat MS

Regulatory T cells are specialised immune cells that play a crucial role in controlling immune responses and preventing autoimmune disease. It has been shown previously that the function of regulatory T cells is altered in patients with MS, such that they are unable to adequately turn off disease-causing self-reactive T cells.

We are investigating the cellular and molecular mechanisms involved in the restoration of functionality and activation of regulatory T cells in experimental autoimmune encephalomyelitis (EAE), a well established murine model of human MS.

The goal of this research is to examine the therapeutic potential for exploiting regulatory T cell activity in the treatment of patients with MS.

In 2008 we successfully generated functional regulatory T cells that possessed integrin molecules. These results suggest that the cells have the ability to migrate to sites of inflammation, and as such, can be used to effectively inhibit experimental MS.

Project Two: The Use of Immunosuppressive Cells to Inhibit EAE

A potent suppressor cell type has been identified that exists as part of the normal immune cell population. These cells are capable of limiting CD4+ T cell responses and are therefore another potential target for the development of therapies to treat autoimmune diseases such as MS.

Using the EAE murine model of human MS, we have discovered that although suppressor cells are present in symptomatic animals, these cells do not possess suppressive activity.

We have identified a compound that appears to have a natural affinity for these suppressor cells and have shown that binding of the compound to this population of cells enhanced their suppressive activity.

When administered *in vivo*, the compound both restored the suppressive activity of the target cells and prevented the development of EAE.

These findings have important clinical implications for the design of novel immunotherapies for the treatment of individuals with MS.

Project Three: Targeting Antigen Presenting Cells to Treat Autoimmune Inflammation

The drug Glatiramer acetate (GA) is currently in clinical use for the treatment of patients with relapsing-remitting MS.

GA is a synthetic mimic of the myelin basic protein that surrounds and protects the nerve fibres of the central nervous system. It is not known exactly how GA works, but it is thought to protect the myelin sheath from T cell mediated damage by acting as a decoy.

We are attempting to further elucidate the suppressive mechanism of GA by identifying the cell type(s) that the drug primarily acts on *in vivo*.

Using our experimental models we have shown that GA is taken up by monocytes after intravenous injection. Interestingly, monocytes exposed to GA demonstrated increased intrinsic T cell suppressive activity, pointing towards a potential mechanism for the observed protective effects of GA.

This information will be vital for the development of strategies that target GA to specific cell types, in order to make the drug more effective.

Assoc Prof Thomas Bäckström (Group Leader)

Assoc Prof Thomas Bäckström, originally from Sweden, established the Multiple Sclerosis Basic Research Group at the Malaghan Institute in 1997 following a one year Postdoctoral research position at the National Jewish Centre, United States of America, and five years as a member at the Basel Institute of Immunology, Switzerland. In 1999 Assoc Prof Bäckström was awarded a five year Wellcome Trust Senior Research Fellowship in Medical Science, and in 2005 he was the recipient of a Wellington Medical Research Foundation's Malaghan Senior Haematology Research Fellowship. Over recent years Assoc Prof Bäckström's research focus has been on identifying mechanisms that inhibit the development and activation of autoreactive T cells. At the end of 2008, Assoc Prof Bäckström left the Malaghan Institute to take up the position of Director of the T Cell Biology Department at Novo Nordisk in Denmark.

PUBLICATIONS

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Andrew KA, Simkins HM, Witzel S, Perret R, Hudson J, Hermans IF, Ritchie DS, Yang J, Ronchese F (2008) Dendritic cells treated with lipopolysaccharide up-regulate serine protease inhibitor 6 and remain sensitive to killing by cytotoxic T lymphocytes *in vivo*. **J Immunol**, 181:8356-62

Baird LJ, Timmer MSM, Teesdale-Spittle PH, Harvey JE Total synthesis of Aigialomycin D using a Ramberg-Bäcklund/RCM strategy. **J Org Chem**, (in press)

Batchelor R, Northcote PT, Harvey JE, Dangerfield EM, Stocker BL (2008) Stereocontrol in carbohydrate chemistry. **J Chem Ed**, 85:689-91

Berridge MV, Herst PM, Lawen A Targeting mitochondrial permeability in cancer drug development. **Mol Nutr Food Res**, (in press)

*Blackie E, Le Ru EC, Meyer M, Timmer MSM, Burkett B, Northcote P, Etchegoin PG (*2008) Bi-analyte SERS with isotopically edited dyes. **Phys Chem Chem Phys**, 10:4147-53

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*Douwes J, Cheng S, Travier N, Cohet C, Niesink A, McKenzie J, Cunningham C, Le Gros G, von Mutius E, Pearce N (*2008) Farm exposure *in utero* may protect against asthma, hay fever and eczema. **Eur Respir J**, 32:603-11

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Grainger R, Taylor W (2008) Establishing outcome domains for evaluating treatment of acute and chronic gout. **Curr Opin Rheumatol**, 20:173-8

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Herst PM, Hesketh EL, Ritchie DS, Berridge MV (2008) Glycolytic metabolism confers resistance to combined all-trans retinoic acid and arsenic trioxide-induced apoptosis in HL60rho0 cells. **Leuk Res**, 32:327-33

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Le Gros G, Ben-Sasson SZ, Seder R, Finkelman FD, Paul WE (2008) Generation of interleukin 4 (IL-4)-producing cells *in vivo* and *in vitro*: IL-2 and IL-4 are required for *in vitro* generation of IL-4 producing cells. **J Immunol**, 181:2943-51

Martin W-J, Walton M, Harper JL Resident macrophages initiating and driving inflammation in a monosodium urate monohydrate crystal-induced peritoneal model of acute gout. **Arthritis Rheum**, (in press)

Mearns H, Horsnell WG, Hoving JC, Dewals B, Cutler AJ, Kirstein F, Myburgh E, Arendse B, Brombacher F (2008) Interleukin-4-promoted T helper 2 responses enhance *Nippostrongylus brasiliensis*-induced pulmonary pathology. **Infect Immun**, 76:5535-42

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Stoitzner P, Green LK, Jung JY, Price KM, Ataera H, Kivell B, Ronchese F (2008) Inefficient presentation of tumor-derived antigen by tumor-infiltrating dendritic cells. **Cancer Immunol Immunother**, 57:1665-73

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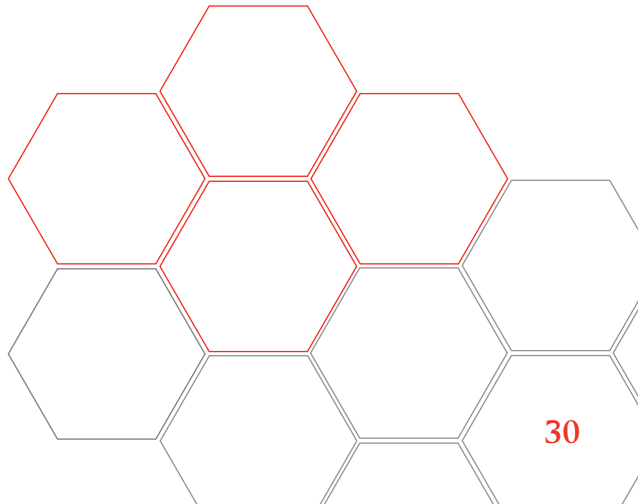
Wang L, van Panhuys N, Hu-Li J, Kims S, Le Gros G, Min B (2008) Blimp-1 induced by IL-4 plays a critical role in suppressing IL-2 production in activated CD4 T cells. **J Immunol**, 181:5249-56

2008 MIMR Patent

Provisional Patent Application filed in New Zealand: 'Synthetic Methods and Compositions'. Emma M Dangerfield, Mattheus SM Timmer and Bridget L Stocker. Reference: 586619 DDG. Filed: 10th October 2008

Full details of all 'in press' publications will appear in the 2009 Annual Report.



February

Asst Prof Søren Skov, Bioinformatics Centre, University of Copenhagen, Denmark. Stress adaptation and the immune response.

MIMR Australasian Society for Immunology (ASI) conference attendees, Malaghan Institute of Medical Research. ASI Sydney 2007 reports.

Invitrogen. Non-antibody based flow technologies.

March

Clare Slaney, Malaghan Institute of Medical Research. The use of myeloid suppressor cells to inhibit EAE: A potential immunotherapy for MS.

Prof Richard Beasley, Director, Medical Research Institute of New Zealand. Is Paracetamol use a risk factor for asthma?

MIMR Group Leaders, Malaghan Institute of Medical Research. Vision for Research in 2008.

April

Prof Len Harrison, Autoimmunity & Transplantation Division, The Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia. Immunity to self co-generates regulatory T cells.

Dianne Sika-Paotonu, Malaghan Institute of Medical Research. Designer vaccines: Increasing the potency of dendritic-cell based vaccines for the treatment of cancer.

Dr Jonathan Wharton, Clinical Sciences Centre, Medical Research Council, London, UK. CD36; accused of many crimes, but where's the evidence?

Dr Anne La Flamme, School of Biological Sciences, Victoria University, Wellington. Regulating activation: Macrophages in autoimmunity.

Haley Ataera, Malaghan Institute of Medical Research. Tregs, tumours & tactics: Investigating the role of Tregs in tumour immuno-evasion.

May

Joel Ma, Malaghan Institute of Medical Research. Elimination of dendritic cells by CD8 cytotoxic T cell and CD4 cell responses.

Prof Philippa Howden-Chapman, Wellington School of Medicine, University of Otago. Keeping warm this winter: Results of the housing, heating and health study.

Nina Dickgreber, Malaghan Institute of Medical Research. Differences in IL-4 production by murine NKT cell subpopulations *in vivo*.

Kylie Quinn, Malaghan Institute of Medical Research. Development and preliminary testing of a novel DNA vaccine against tuberculosis.

Prof Mark Ahn, Professor and Chair, Science & Technology Entrepreneurship, Victoria University, Wellington. New (Ad) Ventures in Biopharmaceuticals: Competing from New Zealand in a global context.

June

New Zealand Branch of the Australasian Society for Immunology Meeting (held at VUW). Keynote speakers: Prof Marc Jenkins, University of Minnesota, USA; Dr Bernadette Saunders, Centenary Institute, Sydney, Australia; Dr Stuart Tangye, Garvan Institute, Sydney, Australia.

Prof Neil Christensen, Laboratory of Experimental Pathology, Penn State Milton S Hershey Medical Centre, Pennsylvania, USA. Model systems to study immunity to papillomavirus infections.

Lisa Connor, Malaghan Institute of Medical Research. BCG-primed lung-resident memory lymphocytes are essential for protection against a lung mycobacterial infection.

July

Prof Steve Henry, Director of AUT Biotechnology Research Institute. Function-Spacer-Lipid KODET constructs (FSL's) changing the face of cell membranes.

Dr Melanie McConnell, Malaghan Institute of Medical Research. Expression of self-renewal genes in glioblastoma tumour-initiating cells.

Dr Gavin Painter, Industrial Research Limited, Lower Hutt. Pattern recognition receptor agonists – Tomorrows adjuvants?

August

Helen Simkins, Malaghan Institute of Medical Research. Fate of CD8+ DC after α-GalCer administration.

Assoc Prof Vic Arcus, Department of Biological Sciences, The University of Waikato, Hamilton. Ancient and contemporary roles for VapBC toxin-antitoxin proteins in bacteria.

Willy-John Martin, Malaghan Institute of Medical Research. Monocytes in acute gouty arthritis.

Prof Bill Denny, Director, Auckland Cancer Society Research Centre, School of Medical Sciences, University of Auckland. Stories of drug development.

September

Marina Harvie, Malaghan Institute of Medical Research. Exploring the key parameters of Th2 protective immunity.

Dr Sarah Hook, School of Pharmacy, University of Otago, Dunedin. Formulation approaches for improving the potency and practicality of subunit vaccines.

Dr Robert Weinkove, Malaghan Institute of Medical Research. NKT cells in chronic lymphocytic leukaemia.

Prof Peter Crampton, Dean, Wellington School of Medicine, University of Otago. The NZDep Index of Socio-economic Deprivation: Development and use 1995 – 2008.

October

Dr Rebecca Grainger, Malaghan Institute of Medical Research. The gout-inflammation project – cellular aspects.

Prof Steven Reiner, Abramson Family Cancer Research Institute and Department of Medicine, University of Pennsylvania, United States of America. Inducing the T cell fates required for immunity.

Tuberculosis New Zealand (TbNZ) meeting. New Zealand's role in global tuberculosis research.

Dr Kylie Hood, Wakefield Gastroenterology Research Institute, Wellington. Laser capture microdissection as a tool for understanding tumour biology.

Prof Parry Guilford, Cancer Genetics Laboratory, University of Otago, Dunedin. Hereditary diffuse gastric cancer: cause, consequence and confidence?

9th International Conference on Membrane Redox Systems: their role in biological stress & disease. Keynote speakers: Prof Gil Mor, Yale University, USA; Prof Bryan Williams, Monash Institute of Medical Research, Australia; Prof John Aitken, University of Newcastle, Australia; Prof Jiri Neuzil, Griffith University, Australia.

Dr Mischa Walton, Malaghan Institute of Medical Research. Macrophages in gout – turning off inflammation with a quick switch?

November

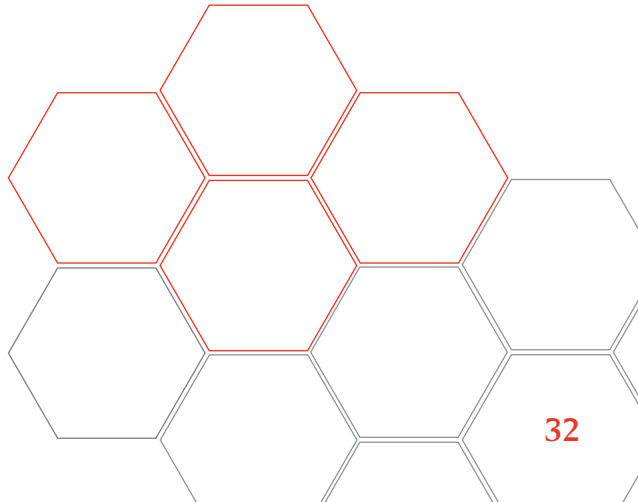
Prof Pierre van der Bruggen, Ludwig Institute for Cancer Research, Brussels Branch, Belgium. Is it possible to correct the anergy of human tumor-infiltrating lymphocytes?

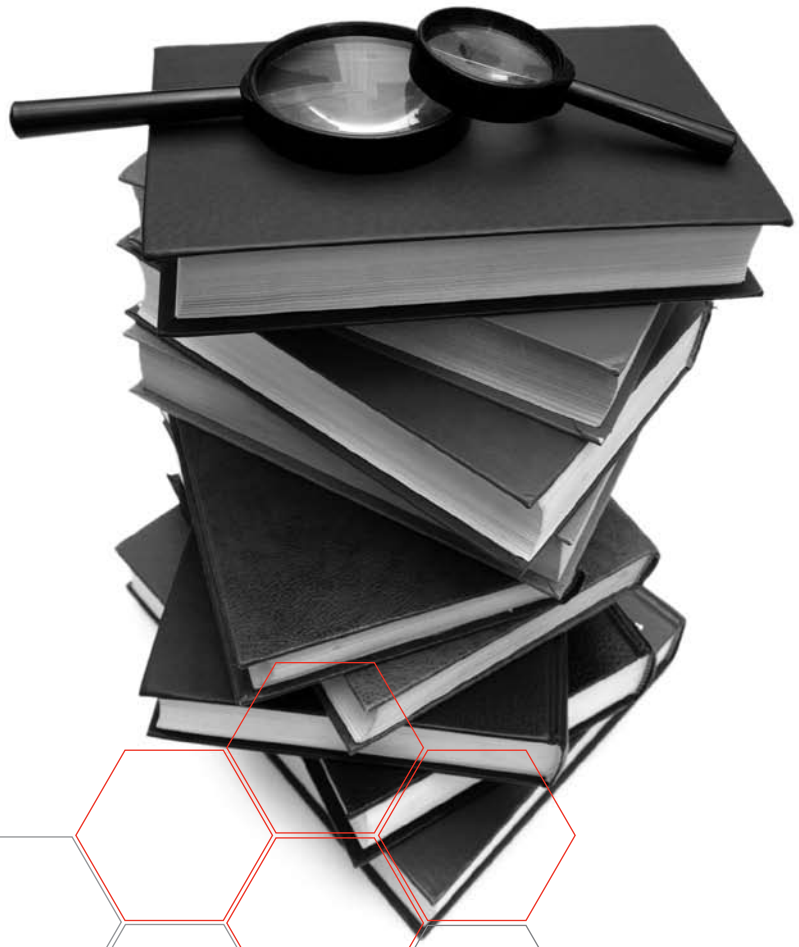
Prof Dale Godfrey, Department of Microbiology & Immunology, University of Melbourne, Australia. Functionally diverse NKT cell subsets.

Assoc Prof Ruth Ganss, Western Australian Institute for Medical Research, Perth, Australia. The "Blood Tumour" barrier: the role of blood vessels during tumour progression and regression.

Emma Dangerfield, Malaghan Institute of Medical Research. Modification of Glycolipids to enhance anti-tumour immunity.

Prof Hans-Georg Rammensee, University of Tübingen, Germany. Patient-individual peptide selection for cancer immunotherapy.





The Malaghan Institute has always had an active commitment to education.

For New Zealand to remain at the forefront of scientific research we require a continuous flow of new, well-trained scientists. At the Malaghan Institute we know that our success is dependent on the calibre of the people who do their research here. For this reason, the Malaghan Institute has 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. To that end, we actively sponsor programmes for doctoral candidates and also provide special opportunities for selected students early in their academic training. We are investing in improving human health by investing in our brightest people and giving them the opportunity to use their skills here in New Zealand.

Doctoral Candidates

In 2008, the Malaghan Institute supported the following PhD students by assigning them to a senior scientist to guide and advise their work. Their studies not only help them satisfy their thesis requirements but also contribute to the core research programmes of the Institute.

Haley Ataera *(BSc, MSc)* "Designing strategies to improve the T cell mediated immunotherapy of mouse tumours"

Lisa Connor *(BBmedSc(Hons))* "Dissecting the long-term memory response against Tuberculosis"

Emma Dangerfield *(BBmedSc(Hons))* "The synthesis of modified carbohydrates for the treatment of disease"

Nina Dickgreber *(DipSci)* "Improving vaccines with adjuvants that stimulate NKT cells"

Marina Harvie *(BSc(Hons))* "Timing and tissue distribution of allergen specific Th2 cells"

Ashna Khan *(BSc, MSc)* "*Mycobacterium tuberculosis* - hijacker of the immune system"

Joel Zhi-Iong Ma *(BSc(Hons))* "Regulation of CD4+ T helper responses by CD8+ T cells"

Willy-John Martin *(BSc, MSc(Hons))* "The role of macrophages in gouty arthritis"

Helen Mearns *(BSc, BSc(Med)(Hons), MSc(Med))* "Role of novel cytokines involved in IL-4 independent Th2 differentiation"

Dianne Sika-Paotonu *(BSc, BBmedSc, MBmedSc(Hons))* "Increasing the potency of dendritic-cell based vaccines for the treatment of cancer"

Helen Simkins *(BSc(Hons))* "Immune responses in perforin deficient mice"

Clare Slaney *(BSc, MSc(Hons))* "The use of immunosuppressive cells to inhibit EAE"

The Malaghan Institute is proud to support three Clinical Research Fellows in their PhD studies.

Dr Peter Ferguson *(MBChB)* "Magnetic nanoparticles as MRI contrast agents"

Dr Rebecca Grainger *(BMedSci(Distinc), MBChB(Distinc), FRACP)* "Immune inflammation in neutrophilic disease – a study of gouty arthritis"

Dr Robert Weinkove *(MA(Hons), MBBS(Hons), MRCPath)* "Invariant natural killer T cells in chronic lymphocytic leukaemia"

The following students had their theses accepted and were awarded their Doctorates in 2008:

Rachel Perret *(BSc(Hons))* "Memory T cells develop from an *in vitro*-activated effector T cell population and can protect against tumours *in vivo*"

Kylie Quinn *(BSc(Hons))* "Development of a novel DNA vaccine to prevent Tuberculosis disease"

Masters Students

In 2008 four students undertook research towards their Masters degrees at the Malaghan Institute.

Kasper Eckert *(BSc)* "Worms and Germs: Do helminth infections impair the efficacy of the tuberculosis vaccine BCG?"

Tommy Liu *(BSc, Grad dip BBmedSc)* "The role of monocytes in gouty arthritis"

Aras Toker *(BSc)* "Targeting antigen presenting cells to treat autoimmune inflammation"

Anna Win *(BSc(Hons))* "Azasugars for the treatment of Tuberculosis"

Honours Students

In continuing our relationship with Victoria University the Malaghan Institute hosted three Honours students in 2008. The research projects were tendered out by the Institute and undertaken by the following successful applicants as a contribution to their Honours study:

Janice Cheng *(BMedSci)* "Glycolipids as adjuvants for anti-cancer immunotherapy"

Gregory Haslett *(BSc)* "The molecular triggers of asthma"

Hannah Kelly *(BMedSci)* "Immunogenicity and protective capacity of DNA vaccines encoding tuberculosis latency antigens"

Visiting Students

The following two international students undertook research at the Malaghan Institute in 2008:

Stefanie Steiger *(DipSci)* "Do activated macrophages phagocytose apoptotic neutrophils?"

Antonia Richter *(BSc, MSc)* "The role(s) of perforin- and Fas ligand- mediated cytotoxicity in the elminiation of dendritic cells"

Summer Students

Each year, the Malaghan Institute hosts summer interns who have an interest in science, and are of the calibre to take on and benefit from an assigned research project at the Institute. Working with close direction from the Institute staff, they are able to conduct meaningful work and learn what a career in research offers. Over the summer of 2008/09, we fostered the following students:

Henry Hudson *(BMedSci (3rd year))* "Effect of different cations on immune responses to urate crystals"

Neal Kerr *(BSc (3rd year), MBChB (3rd year))* "The effect of high uric acid on MSU induced superoxide production by human neutrophils"

Taryn Osmond *(BBmedSc)* "Stress-related gene expression in cancer cells and immune cells"

Catherine Plunkett *(BMedSci)* "Imino sugars as inhibitors of *Mycobacterium tuberculosis* – synthesis and biological evaluation of a new class of Mycobacterial arabinan biosynthesis inhibitors"

Sarrabeth Stone *(BBmedSc)*

Community Education

At the Malaghan Institute, we are dedicated to disseminating the knowledge gained through our research to the community. In 2008, we had 14 community groups tour the Institute. The groups had the opportunity to meet the Malaghan Institute's internationally acclaimed scientists, learn about the immune system and experience medical research in action. In addition our staff gave presentations to 16 clubs, community groups and schools offsite.

FUNDRAISING REPORT

All the funds raised go directly towards supporting the scientists and their vital research goals of finding better treatments and cures.

As Fundraising & Communications Manager of the Malaghan Institute of Medical Research I am very proud to be part of a wonderful team who are raising both vital funding and awareness of the Institute here in New Zealand. We have a fantastic office team here in Wellington and we are also very lucky to have over 30 dedicated volunteers on our Friends committees, as well as hundreds of other helpers for our events.

2008 was a stellar year for the Fundraising department and what better way to showcase this than with some interesting facts:

- Approximately $45,000 was raised from the Lollipop Street Appeal in February
- To collect that money, over 250 volunteers hit the streets of the Greater Wellington region with collection buckets and lollipops
- 14 tour groups visited our facilities to see first-hand the work carried out here
- 16 community groups were visited by one of our scientists
- Over $200,000 was received in donations via our three mail appeals during the year
- To reach this total, approximately 2,600 people sent in donations
- Collectively, the Charity Golf Tournaments organised by the Friends Committees raised over $100,000

From this we can conclude that we are very lucky indeed to have such wonderful donors, volunteers and supporters of our work!

All the funds raised go directly towards supporting the scientists and their vital research goals of finding better treatments and cures for cancer, asthma, arthritis, MS and infectious disease. Without this financial assistance, the research would stop, so thank you very much to all of you who have shown your commitment to our organisation this year.

Tanya Fulcher, Ashley Hallsmith, Dr Debbie Scarlett, Jacqui Whelan

FUNDRAISING AND COMMUNICATIONS

FRIENDS OF THE MALAGHAN INSTITUTE

Thank you to the following people – all of whom give amazing amounts of time to fundraising for the Malaghan Institute of Medical Research. You are all truly appreciated.

Wellington Friends

Robyn Vavasour (Chair)
Judy Blair
Adrienne Bushell
Maureen Cameron
Gaye Carroll
Sylvia Goldman
Jill Kinloch
Susan Laurenson
Emma Lawler
Jill Strang
Denise Udy

Wellington Fundraising Functions 2008

Lollipop Street Appeal
Wellington Friends 21st Birthday Cocktail Reception
ING NZ Ltd Malaghan Golf Tournament

Hawkes Bay Friends

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Beth Kay
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Hawkes Bay Fundraising Functions 2008

Malaghan Institute Golf Tournament

Auckland Friends

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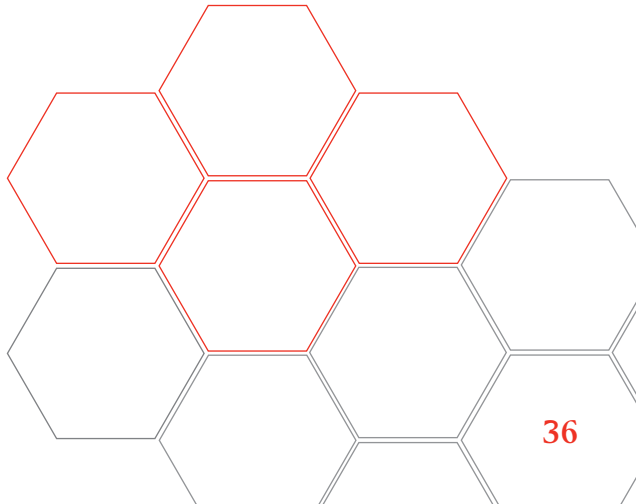
Mary Collow
Steve Culpan
Elaine Haggitt
Margaret Malaghan
Penny Rennell
Raewyn Roberts
Jo Whale

Auckland Fundraising Functions 2008

AMI Insurance Malaghan Golf Tournament



Thank you to the following individuals, organisations, businesses, Trusts and Foundations who helped support the Malaghan Institute in 2008:

Grants, Trusts and Foundations

Arthritis New Zealand
Arthur N Button Charitable Trust
Cancer Research Charitable Trust
Cancer Society Wellington Division
Cancer Society of New Zealand
Caversham Foundation
Cuesports Foundation Ltd
Foundation for Research, Science & Technology
Genesis Oncology Trust
Harry and Beverley Romanes
H B Williams Turanga Trust
Health Research Council of New Zealand
Infinity Foundation Ltd
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Marjorie Barclay Trust
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Maurice Wilkins Centre for Molecular Biodiscovery
Melanoma Research Alliance
Morris Cancer Research Foundation Trust
New Zealand Community Trust
New Zealand Lottery Health Research
Nikau Foundation (previously Wellington Region Foundation)
Pub Charity Ltd
Rex and Betty Coker
Roy McKenzie
SE Leuchars Family Trust
Sir Roy McKenzie Industrial Research Ltd Charitable Trust
Springhill Charitable Trust & Frimley Foundation
The Keith Taylor Charitable Trust
The Royal Society of NZ Marsden Fund
The Southern Trust
Thomas George McCarthy Trust
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Victoria University of Wellington
Wellington Medical Research Foundation

Corporate Supporters

AMI Insurance
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Bayleys Real Estate
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Black Barn Vineyards
Blair Gowrie Investments Ltd
Botanical Skin Care
Boulcott Street Bistro
Bourke Contracting
BP OIL NZ Ltd
Brian Setter
Brittain Wynyard & Co Ltd
Brooklands Land Co.
Business World Travel
Cable Bay Restaurant
Cadbury Confectionary Ltd
Caffe L'affare
Cameron & Partners
Cape Kidnappers Golf Club
Cape Physio Ltd
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Cedon Apparel
Ceroc Dance
Chop Hairdressers
Coca Cola Amatil Ltd
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Colin Blair
Connells Bay Sculpture Park
Cre@ive Design Advertising
Craggy Range Winery
Cricket Wellington
Datamail
Datastor NZ Ltd
Delmaine Fine Foods ltd
Di Conway
Diva Restaurant and Bar
Dr Steve Culpan
Dunallstair House
Edward Memarne Hair & Beauty
Elizabeth Horne
Esteem Jewellery
Eurowine
Farmlands Trading Society
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Forbes & Co.
Freyberg Pool & Gym
Fuji Xerox
GDL Brands
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Golf Club NZ
Golf Today Ltd
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Greenfernz
Hastings Golf Club
Hawkes Bay Insurances
Hill Seekers
Holiday Inn, Wellington
Hotel Intercontinental

FUNDING SOURCES

HSBC
Hummingbird Café and Bar
Hynds Pipe Systems Ltd
Industrial Processors
Inspire Photography
ING (NZ) Ltd
Jeff Gray BMW
John Balmforth
John Holt Memorial Trust
John Pinel Memorial
Kapiti Oil
Kiely Thompson Caisley
Kinloch Golf Resort
Le Metropolitain French Bistro
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Manor Park Golf Club
Maria Gourlie
Martin Bosley's Yacht Club Restaurant
Matangi Cottages
Matariki Wines Ltd
Maxwell's Golf Retreat
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Mudgway Parts World
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New Zealand Symphony Orchestra
NOW Couriers
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Olive Tree Café
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Opus International Consultants Ltd
Oracle NZ Ltd
Orton Catering Ltd
Pak n Save, Hastings
Parker and Associates
Parawai Lions Club
Pearson Investment Advisory Ltd
Port of Napier
Porter Hire Ltd
Pru McKenzie
Rainbow Print
Rapp Collins Walker
Regional Health
Renaissance Ltd
Rennells Jewellers & Engravers
Resene Paints Ltd
Richard Laurenson
Ruapehu Golf & Country Lodge
Rutherford & Bond Toyota
Samson & Delilah Beauty Salon
Saunders Unworth
Sconnor
Senate Communications
Signwise Auckland Ltd
Sileni Estates
Simpson Grierson
Smith & Smith Ltd
Spy Valley Wine
Stagecoach
Strawberry Fare Restaurant
Swarovski International (NZ) Ltd
Tessa Chambers
The Beleza Co Ltd
The Cut Magazine
The Diamond Shop
The Grange Golf Club
The Terrace Conference Centre
The Village Press Ltd
The White House Restaurant
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Turners & Growers Ltd
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Urban Sanctuary
Valley Printing, Petone
Vavasour Wines
VetEnt Wairoa
Vista Restaurant
W Stevenson & Sons Ltd
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Wairunga Golf Course
Wakefield Health Ltd/Royston Hospital
West Plaza and Bay Plaza Hotels
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Special Donors

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Bequests

Gordon Anderson
BEA Trust
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Walter A Clark
Trevor Davey
David Ferguson
Malaghan Family
Marion Mitchell
H Mossman
Maureen Mullany
Dr Margaret Neave
Ernest Robinson
Thelma Wood

In Memoriam Donations

Donations were received in memory of the following people:

Margaret Aiken
Bryan Ambler
Martin Collins
Grant W Fowles
Patricia Fyfe
Robert John Gilbert
Don Hamlin
Margaret Jamieson
Neville Jones
Joyce Macdougall
Coleen McMorran
Paul M Nevin
Heather M Northover
Jillian Ryan
Miriam Smith
Jill Strang
Dr Harry Swadling
Graeme Thomson
Kenneth Alan Tweedale
Guy Zink

How can you help us lick Cancer, Asthma, Arthritis, MS and Infectious Disease?

The Malaghan Institute is independent and receives no direct government funding. It is 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. We have the most committed and qualified team of scientists working around the clock on the toughest, and most urgent, human diseases. We are making good progress toward the ultimate goal of developing effective treatments and vaccines for some of the world's most dangerous and debilitating diseases, but without funding the work will stop and this will be unattainable.

The Malaghan Institute is a registered charity and any support is gratefully received. Please support our vision by investing in health for the benefit of all New Zealanders.

The following are some options for supporting medical research at the Malaghan Institute of Medical Research.

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 are happy to recognise support in a way that is appropriate to our sponsors.

HOW YOU CAN HELP

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 a 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) or

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.

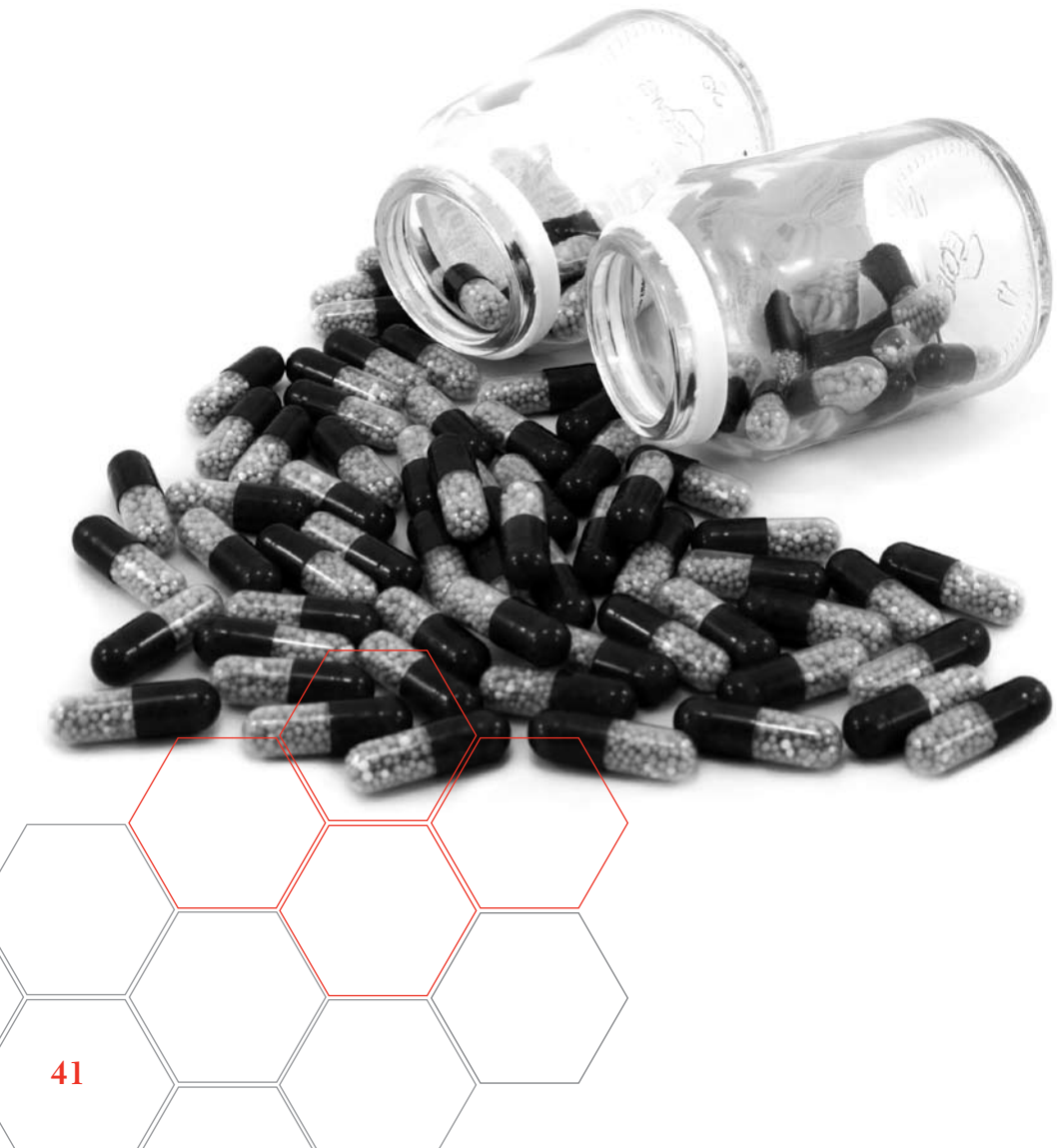
Should you require any additional information or have any queries, please contact:

Fundraising and Communications Manager
Malaghan Institute of Medical Research

PO Box 7060
Wellington 6242
New Zealand
Ph: +64 4 499 9614

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

FINANCIAL REPORT



Despite the difficult economic times our donors continue to support us.

The 2008 year has been a favourable one with our scientific research progammes benefitting from good funding from contestable grant applications.

Despite the difficult economic times our donors continue to support us, albeit at a reduced level.

Depreciation for the year is $668k and continues to be the largest component of our operating deficit. We spend our cash on research and have again been fortunate this year in securing $1.1m to fund new and replacement assets.

The Capital Endowment Fund has also taken a writedown, albeit unrealised, in these uncertain economic times, the values have declined a further $128k since our balance date. Our investments are blue chip and our Investment Committee has decided to continue to hold these and ride out the storm. New funding has been channeled into investment grade bonds. This strategy will continue for the 2009 year.

Susie Whelan, Janine Gray

FINANCE

AUDIT REPORT

Deloitte.

TO THE TRUSTEES OF MALAGHAN INSTITUTE OF MEDICAL RESEARCH

We have audited the summary financial statements of the Malaghan Institute of Medical Research and Group for the year ended 31 December 2008 as set out on pages 43 & 44.

Trustees' Responsibilities

The Trustees are responsible for the preparation of summary financial statements in accordance with New Zealand law and generally accepted accounting practice.

Auditors' Responsibilities

It is our responsibility to express to you an independent opinion on the summary financial statements presented by the Trustees.

Basis of Opinion

We conducted our audit in accordance with New Zealand Auditing Standards. We planned and performed procedures to ensure the summary financial statements are consistent with the full financial statements on which the summary report is based. We also evaluated the overall adequacy of the presentation of information in the summary financial statements against the requirements of FRS-43: Summary Financial Statements.

Other than in our capacity as auditor, we have no relationship with or interests in Malaghan Institute of Medical Research and Group.

Qualified Opinion

Control over the revenues from donations, bequests and grants prior to being recorded is limited, and there are no practical audit procedures to determine the effect of this limited control. As a result, Malaghan Institute of Medical Research and Group's full audited financial statements contained a qualified audit opinion.

In our opinion, the information reported in the summary financial statements complies with FRS-43: Summary Financial Statements and is consistent with the full financial statements from which it is derived. We expressed the qualified opinion referred to above in our report to the Trustees dated 11 March 2009.

For a better understanding of the scope of our audit of Malaghan Institute of Medical Research and Group's financial statements and of Malaghan Institute of Medical Research and Group's financial position, financial performance and cash flows for the year ended 31 December 2008, this report should be read in conjunction with Malaghan Institute of Medical Research and Group 's audited financial statements for that period.

Our examination of the summary financial statements was completed on 11 March 2009 and our qualified audit opinion is expressed as at that date.

Deloitte

Chartered Accountants

WELLINGTON, NEW ZEALAND

Malaghan Institute of Medical Research - Summary Accounts 2008

Consolidated Statement of Financial Performance For year ended 31 December	2008 Consolidated	2007 Consolidated
Income - Operating		
Income from Donations	592,166	755,894
Income from Scientific Grants	4,638,101	4,376,734
Interest and Income from Investments	379,531	133,873
	5,609,798	5,266,501
Expenses - Operating		
Salaries	3,010,379	2,585,693
Expenses (including depreciation)	3,515,466	3,379,728
	6,525,845	5,965,421
Operating (Deficit)	**(916,047)**	**(698,920)**
Plus Grant Income for Fixed Asset Purchases	1,100,834	115,324
Net Surplus/(Deficit)	184,787	(583,596)
Capital Endowment Fund		
Income		
Investment Income	(185,979)	218,394
Bequests	580,850	312,731
Net Income	394,871	531,125

FINANCIAL ACCOUNTS

Consolidated Statement of Movements in Equity For year ended 31 December	2008 Consolidated	2007 Consolidated
Opening Balance	5,797,862	5,850,333
Net surplus/(deficit) for the year		
- Operating Income	184,787	(583,596)
- Capital Endowment Fund	394,871	531,125
Total recognised income and expenditures	579,658	(52,471)
Total Funds	6,377,520	5,797,862

Consolidated Statement of Financial Position As at 31 December	2008 Consolidated	2007 Consolidated
Current Assets	5,060,372	5,132,612
Less Current Liabilities	3,115,680	2,990,802
Plus Fixed Assets	1,833,565	1,326,027
Plus Investments	2,599,263	2,330,025
Total Equity	6,377,520	5,797,862

Consolidated Statement of Cash Flows For year ended 31 December	2008 Consolidated	2007 Consolidated
Net Cash Flow from Operating Activities	1,855,213	475,626
Net Cash Flow from Investing Activities	(1,747,767)	(717,880)
Net Cash Flow from Financing Activities	-	-
Net Increase in Cash Held	107,446	(242,254)
Cash at Beginning of the Year	2,320,262	2,562,516
Cash at End of the Year	2,427,708	2,320,262

Presented on page 43 and 44 are the Summary Financial Statements of the Malaghan Institute of Medical Research (the "Institute"), a not for profit entity, for the year ending 31 December 2008 which were extracted from the full Financial Statements authorised for issue by the Trust Board on 11 March 2009. An qualified audit report was issued on 11 March 2009.

As the summary Financial Statements do not include all the disclosures that are in the full financial Statements, it cannot be expected to provide as complete an understanding as produced by the full Statement of Financial Performance, Financial Position and Cash Flows. These Summary Financial Statements are in Compliance with FRS-43: Summary Financial Statements, and are presented in New Zealand Dollars (NZD).

A copy of the full financial statements can be obtained from the Financial Manager, Malaghan Institute of Medical Research, P O Box 7060, Wellington South, New Zealand.

BOARD OF TRUSTEES

Graham Malaghan *FCILT (Chairman)*

John Beattie *LLB (VUW)*

Prof David Bibby *DSc(Loughborough University)*

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Bryan Johnson BCA*(VUW)*

Prof Graham Le Gros *BSc (Massey), Dip Immunol(Otago), MPHIL(Auck), PhD(Auck), FRSNZ*

Matthew Malaghan *BCom(Otago), MCIT (from Aug)*

David Mossman *BVSc, MRCVS, MNZIF*

Gary Quirke *BCA, CA, FCILT*

Dr Jim Watson *PhD(Auck)*

C Dan Williams *CA*

STAFF OF THE INSTITUTE 2008

Scientific

Director of Research

Prof Graham Le Gros *BSc(Massey), Dip Immunol(Otago), MPhil(Auck), PhD(Auck), FRSNZ*

Group Leaders

Assoc Prof Thomas Bäckström *BSc(Hons)(Stockholm), PhD(Auck) – Wellington Medical Research Foundation Malaghan Haematology Fellow (to Aug)*

Prof Mike Berridge *BSc, MSc(Hons), PhD(Auck)*

Dr Jacquie Harper *BSc(Hons), PhD(Otago)*

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Dr Joanna Kirman *BSc(Hons), PhD(Otago)*

Prof Franca Ronchese *PhD(Padua), Dip Microbiology*

Dr Bridget Stocker *BSc(Hons), PhD(VUW)*

Research Associate

Dr Anne La Flamme *BS(MIT), MS, PhD(Washington) (from Aug)*

Senior Research Fellows

Dr Melanie McConnell *BSc(Hons), PhD(Otago)*

Dr Mattie Timmer *MSc, PhD (Leiden, Netherlands) (P/T)*

Research Fellows/Post-doctoral Research Fellows

Dr Lynton Baird *BSc(Hons)(Otago), PhD(VUW) (from Jun)*

Dr Noriyuki Enomoto *MD, PhD(Hamamatsu, Japan)*

Dr Elizabeth Forbes *BSc(VUW), PhD(ANU)*

Dr Rachel Perret *BSc(Hons), PhD(Otago) (Jun to Dec)*

Dr Troels Petersen *MSc, PhD(Copenhagen) – Regulatory Affairs Officer*

An Tan *BSc(VUW)*

Dr Nicholas van Panhuys *BSc(Hons)(VUW), PhD(Otago) (to Apr)*

Dr Mischa Walton *MSc(Friedrich-Schiller, Germany) PhD(Massey) (from Mar)*

Staff Scientists

Evelyn Bauer *NZCSc, Cert Animal Sci & Tech(Massey) – GMP Production Technician*

Nicola Kofoed *BSc, DipGrad(Otago) – Manager BRU*

Kylie Price *BSc(Otago), MSc(Hons)(VUW) – Flow Cytometry Suite Manager*

Xiaodong Wang *Dip Med Tech, Dip Midwifery(Shanxi)*

Senior Research Officers

Mali Camberis *BSc(VUW)*

Kathryn Farrand *MSc(Massey)*

Melanie Prout *BSc(Hons)(VUW)*

Fenella Rich *BSc(Hons)(Otago), DPH(distinc)(Otago)*

Evelyn Spittle *MSc(Distinc)(Otago)*

Dr Jianping Yang *MB(Shanxi Medical University)*

Research Officers

Kate Broadley *BSc(Massey)*

Susanna Brow *BSc, BMedSc(VUW) (P/T) (to Sep)*

Clarissa Chandrahasen *BBmedSc(VUW)*

Carole Grasso *BSc(Hons)(West of England) (P/T)*

Deborah Knight *MSc(Otago) (from Jul)*

Brigitta Mester *MSc(Hungary)*

Dr Ben Mulchin *BScTec(Hons)(VUW), PhD(Massey) (from Apr)*

Jim Qin *BSc(Hons)(Auckland) (to Jan)*

Shiau-Choot Tang *Grad Dip Sci(VUW)*

Dr Mischa Walton *MSc(Friedrich-Schiller, Germany) PhD(Massey) (to Mar)*

Research Assistants

Sharon Brokenshire

Amy Doyle *BSc(VUW)*

Stephanie Huck *BSc(Massey) (P/T)*

Kelly Locke

Katherine MacGregor *BSc(Massey)*

Amanda Payne *BSc(Otago)*

Research Nurse

Catherine Wood *RN, BN(Whitireia), PGDipHealSci(Otago)*

Visiting Researchers

Dr Scott Harding *MBChB(Otago), FRACP (P/T)*

Dr Patries Herst *BSc, MSc(Netherlands), MPhil(Waikato), PhD(Otago) (P/T)*

Dr Anil Ranchord *MBChB(Otago)*

Clinical Research Fellows

Dr Peter Ferguson *MBChB(Otago) (from Apr)*

Dr Rebecca Grainger *BMedSci(Distinc), MBChB(Distinc) (Otago), FRACP*

Dr Robert Weinkove *MA(Hons)(Cantab), MBBS(Hons) (London), MRCPath(UK)*

PhD Students

Haley Ataera *BSc, MSc(VUW)*

Lisa Connor *BmedSc(Hons)(VUW)*

Emma Dangerfield *BBmedSc(Hons)(VUW) (from Jan)*

Nina Dickgreber *DipSci(Kiel)*

Marina Harvie *BSc(Hons)(VUW)*

Ashna Khan *BSc, MSc(VUW) (from Dec)*

Joel Zhi-long Ma *BSc(Hons)(NUS, Singapore)*

Willy-John Martin *BSc, MSc(Hons)(Waikato)*

Helen Mearns *BSc, BSc(Med)(Hons), MSc(Med)(UCT) (from Feb)*

Rachel Perret *BSc(Hons)(Otago) (to Jan)*

Kylie Quinn *BSc(Hons)(Otago) (to Jun)*

Dianne Sika-Paotonu *BSc, BBmedSc, MBmedSc(Hons)(VUW)*

Helen Simkins *BSc(Hons)(Otago)*

Clare Slaney *BSc, MSc(Hons)(Auckland)*

Masters Students

Kasper Eckert *BSc(Copenhagen) (to Mar)*

Tommy Liu *BSc(Otago), Grad dip BBmedSc(VUW) (from Mar)*

Aras Toker *BSc(WWU Münster, Germany)*

Anna Win *BSc(Hons)(VUW) (from Jul)*

Honours Students

Janice Cheng *BMedSci(VUW)*

Gregory Haslett *BSc(VUW)*

Hannah Kelly *BMedSci(VUW)*

Visiting Students

Stefanie Steiger *DipSci(MLU, Germany) (from Apr)*

Antonia Richter *BSc(TUM, Germany) (from Aug to Oct)*

Summer Students 2008/2009 (Nov-Jan)

Henry Hudson *BMedSci(VUW) (3rd year)*

Neal Kerr *BSc(Otago) (3rd year), MBChB(Otago) (3rd year)*

Taryn Osmond *BBmedSc(VUW)*

Catherine Plunkett *BMedSci(VUW)*

Sarrabeth Stone *BBmedSc(VUW)*

Research Consultants

Assoc Prof John Carter, Wellington Cancer Centre

Prof Chris Cunningham, Te Pümanawa Hauora, School of Māori Studies, Massey University

Prof Brett Delahunt, University of Otago

Prof Keith Grimwood, Dept of Paediatrics and Child Health, Wellington School of Medicine & Health Sciences

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

Mr Martin Hunn, Wellington Hospital

Dr David Ritchie, Peter MacCallum Institute, Melbourne, Australia

Science Support and Administration

Administration

Carolyn Hallsmith - *Receptionist (P/T)*

Finance

Janine Gray *BCA(VUW) – Assistant Accountant (P/T)*

Susie Whelan *CA, NZIMDip – Finance Manager*

Fundraising

Tanya Fulcher *BSc(VUW) – Fundraising & Communications Manager*

Ashley Hallsmith *BBmedSc(VUW) – Fundraising Assistant (P/T) (to Oct)*

Dr Debbie Scarlett *BSc(Hons), PhD(Otago) – Science Communications Advisor (P/T)*

Jacqui Whelan – *Fundraising Assistant (P/T)*

Operations

Charlotte Cheriton – *Administration Manager BRU*

Laurence Fallon – *Laboratory Assistant*

Andrew Hamer-Adams – *IT Support (from Sep)*

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

Darrell Smith *MSc(Hons)(VUW), (Dip A.T.)(Wgtn Polytech), BSA(Massey) – Facilities Manager*

Mark Williams – *IT Assistant (P/T) (to Nov)*

Michal Zablocki *BA(Hons)(Bristol) – Chief Operating Officer*

PA to Director (Human Resources)

Gabrielle Dennis *RSA(English), Pitmans*

ADVISORS

Auditors

Deloitte

Bankers

The National Bank

Investments

David Wale

Solicitors

Simpson Grierson

MALAGHAN INSTITUTE OF MEDICAL RESEARCH

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Victoria University, Entrance 7, Kelburn Parade, Wellington
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