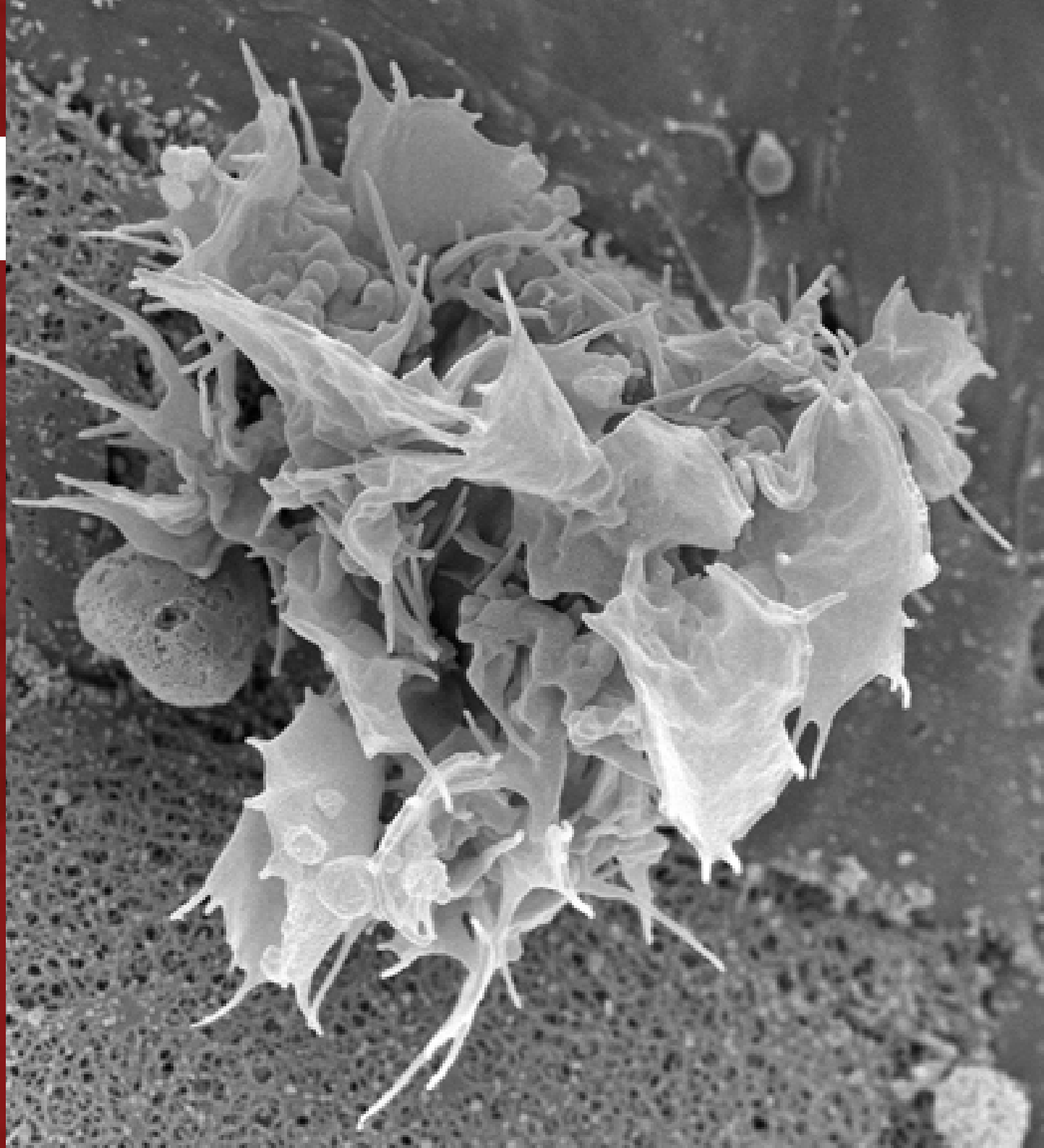
MALAGHAN INSTITUTE OF MEDICAL RESEARCH

ANNUAL REPORT 2009/10



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ABOUT US

The mission of the Malaghan Institute is to improve the human condition through biomedical research.

The Malaghan Institute of Medical Research is New Zealand's leading 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 to 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 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, whilst still preserving our independent status, the Institute works closely with tertiary institutions, Crown Research Institutes, hospitals and clinics throughout New Zealand.

This 2009/10 Annual Report covers the period 1 January 2009 – 31 July 2010, excluding the Financial Accounts, which cover the period 1 August 2009 – 31 July 2010. We hope you enjoy reading about all of the tremendous developments that have taken place during this time.

CHAIRMAN'S REPORT

I recently took the opportunity to revisit the last few years' Annual Reports, particularly my own comments within them. Many of the concerns and opportunities I discussed in previous years are as valid today as they were then. As the old adage goes, the more things change, the more they stay the same. While the Malaghan Institute has certainly changed, the environment in which it operates is still dealing with the same challenges.

Our research programme continues to gain strength. Our efforts in the last year, led by the Director Prof Graham Le Gros, are well highlighted both in his report and throughout this document. Prof Le Gros' leadership was recognised in September this year at the 50th anniversary of the Wellington Medical Research Foundation, where he was awarded one of only two medals for outstanding contributions to research. New Zealand is the richer for the excellent work being done by our researchers. They provide hope that solutions to suffering can and will be found. Our role as Trustees is to ensure they have the resources and facilities to maintain their efforts.

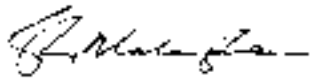
We embarked a couple of years ago on a programme to grow our financial strength through our Capital Endowment Fund and thereby achieve the security needed for future endeavours. We have not made the progress I would have hoped, but then again we have had some wonderful financial support to provide facilities and maintain operations during that same period. We also drew on our own Capital Endowment Fund to support the construction of our new cancer laboratories. This is why such funds are vital, they allow Trustees to support the research teams' needs when other sources of funding are not available at the time. Over the next year we will be further resourcing our development and fundraising team and seeking to increase awareness, throughout the country, of the national asset that the Institute represents. In doing so we will renew the appeal to grow our Endowment Fund and ongoing support for the scientific programmes.

Since our last report we have commissioned a major review of the focus and performance of our science programme. A panel of three highly experienced researchers, two of whom were from Australia, gave the Director and his team full marks for the quality and direction of their work. They also noted that the success of our researchers to date has been quite outstanding, given the relative paucity of financial resources available to them. We will ensure that this process of independent review continues; it provides a valuable oversight and also adds considerable support to our research leaders.

During the past fifteen months I have spent considerable time seeking to establish a new voice for the promotion of health research in the wider community. This prospective association of health research stakeholders obtained the support of philanthropic organisations, the pharmaceutical industry and universities. It also secured financial commitments for the forthcoming three year period to fund an executive team. However, the initiative foundered when the two main health research universities withdrew their support. I am disappointed that we were unable to get the venture off the ground as I believe New Zealand needs a strong, consistent voice promoting health research. However, the Malaghan Institute and other like-minded organisations will maintain our efforts to increase awareness of the value of health research in New Zealand. In order to meet the challenges we all face, more than one voice is necessary in this arena.

I must make special mention of the Health Research Council of New Zealand, who recently approved funding for three major projects of work for our researchers; also Victoria University, which continues its unwavering support and is a great host of our endeavours; and lastly AMI Insurance, who continue to inspire us with their commitment to the Institute.

To all our supporters, donors, Friends group members, Trustees and staff I again commend you for your unflagging work and energies in promoting the Institute.



Graham Malaghan

CHAIRMAN

DIRECTOR'S REPORT

In 2009 the Malaghan Institute celebrated its 30th anniversary. Reflecting back on my time here, I have seen this organisation grow from a small but dedicated team of a dozen scientists to a multi-skilled, cross-disciplinary staff of nearly one hundred. Our overriding goal – to realise genuine health outcomes from our basic research – has driven this growth as we have established new research teams and launched an ambitious course of clinical trials. The nineteen months since our last annual report was published have followed the same pattern. We have established a new group investigating the mechanisms of cell death and their role in diseases such as cancer and motor neurone disease. We have added a new clinical laboratory suite to our facility that will allow us to expand our programme of clinical trials and vaccine development. We have also been extremely successful in securing research funding this past year from the HRC to undertake new initiatives in the areas of cancer, asthma and allergy, and arthritis research, and vaccine development against the infectious diseases tuberculosis and human hookworm.

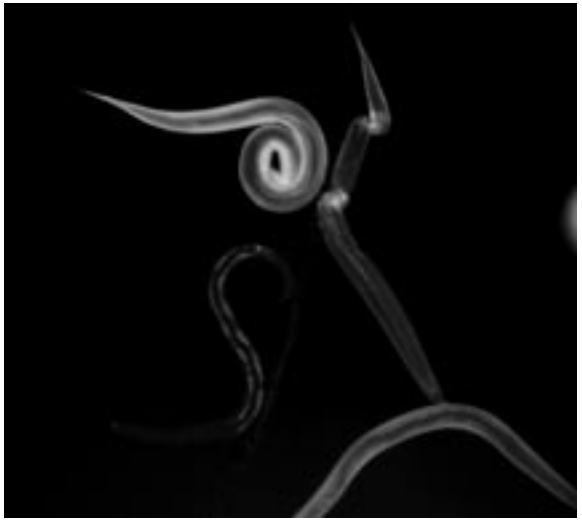
A particular feature of our research endeavours is that they have been strongly supported over the years by an extensive network of New Zealand and international collaborators. Breakthroughs are now rarely achieved in isolation and the exchange of cutting edge technologies and ideas is essential for the good health of the Malaghan Institute science programmes. In this regard it is pleasing to acknowledge the many new and high profile collaborations that were established this last year.

Research Highlights

This year our research initiatives achieved major success in the Health Research Council of New Zealand funding round. As a result we have commenced three exciting new programmes: Firstly, a promising new formulation of our cancer vaccine will be trialled against melanoma – a project led by Dr Ian Hermans and jointly undertaken with The University of Auckland, the Maurice Wilkins Centre, Industrial Research Limited and the Wellington Blood and Cancer Centre. Secondly, Prof Franca Ronchese will be investigating the potential of exploiting cytotoxic T-lymphocytes, which her group has shown to play an important role in suppressing cancer vaccine induced immune responses, to prevent the development of asthma. Thirdly, my own Parasitology team will be taking our discovery that instigating an immune response in the lung can prime effective immunity against migrating parasitic worms (see image) to work towards a vaccine for human hookworm – a disease that affects one billion people worldwide.

These three research initiatives all point towards a rapidly maturing capability at the Malaghan Institute – vaccine development. Given our historical focus on immunology, this is a natural progression as we continue to use what we have learned in the laboratory to form the basis of new treatments and therapies for patients.

This philosophy of undertaking research with direct clinical outcomes was also present in two other recent projects. In 2009 we commenced our phase I clinical trial of a cancer vaccine against glioblastoma multiforme – a highly aggressive brain tumour. Led by Dr Ian Hermans and Mr Martin Hunn, a neurosurgeon from Wellington Hospital, this trial is now well underway and offers hope to patients with few remaining options available among conventional therapies. Also in 2009 we launched a new research programme into breast cancer. Funded by the Breast Cancer Research Trust and headed by Prof Mike Berridge, with support from Dr Melanie McConnell and Dr Troels Petersen, the programme aims to combine our strengths in immunotherapy and cell metabolism to investigate the potential for a vaccine against the disease. It is hoped that we will be able to begin a clinical trial against breast cancer by 2013.



Nippostrongylus brasiliensis larvae - a rodent parasite model of human hookworm (see pg37 for more information on this research)

One of the unique assets we have at the Malaghan Institute is our Immunoglycomics team who, under the leadership of Dr Bridget Stocker, bring a fusion of chemistry and immunology expertise to tackling disease. This year, in addition to their invaluable research, they also developed a novel way of producing iminosugars, a class of drugs used to treat a variety of diseases. This methodology, through use of water and ethanol instead of petrol, is much more efficient and ecological than previous techniques. This innovation was shortlisted for a Wellington Green Gold Award in 2010 and could potentially lead to 'greener' drug production worldwide.

There were numerous accomplishments by our staff over the past year that I would like to recognise. Firstly, I congratulate Dr Melanie McConnell on establishing her own research team, investigating mechanisms of cell survival. Dr Joanna Kirman was elected president of the New Zealand division of the Australasian Society for Immunology. Prof Ronchese was nominated to represent Australasia on the International Union of Immunological Societies and, as mentioned above, Dr Stocker was shortlisted for a Wellington Gold Award. These accolades are indicative of both the strength of our research team, and their contribution towards the wider research environment.

Our scientists have also frequently appeared in the media, with Dr Hermans, Prof Berridge, Dr Kirman, Dr McConnell, Mali Camberis and Kylie Price, our Flow Cytometry Manager, all giving interviews for TV and radio.

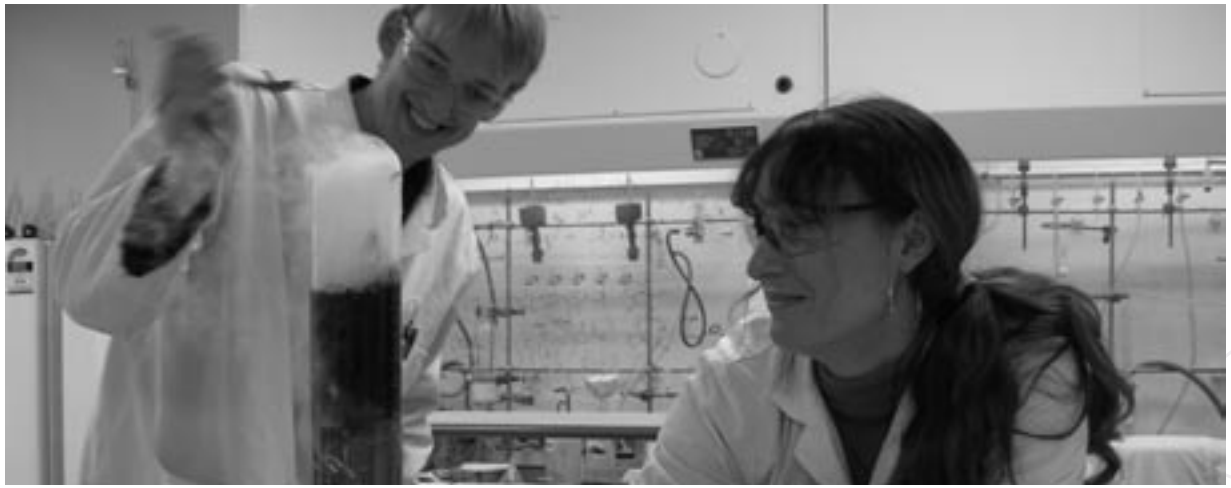
Operations

In order to support our growing research platform our Operations staff have had a particularly busy year. In May 2010 we officially opened the Keith and Faith Taylor Cancer Research Laboratories – a dedicated suite of laboratories designed for vaccine development. Built to meet the rigorous GMP (Good Manufacturing Practice) standards required for working with human materials, this facility represents our long-term commitment towards developing cell-based therapies against disease. My thanks go to both Victoria University of Wellington, for their unstinting support and shared vision for our future, and to the Taylor Family for their generosity in helping us establish these laboratories.

I would also like to recognise the efforts of Darrell Smith, our Facility Manager, and Evelyn Bauer, our Clinical Trials Manager, in tailoring this facility so precisely to our needs.

Another area of significant growth at the Malaghan Institute has been our Flow Cytometry Suite, which has undertaken a recent Biosafety Upgrade. This means that Flow Cytometry Manager Kylie Price can now use the cell sorter to work with potentially infectious cells, or isolate immune cells from patients, something we haven't been able to do up until now because of the risks associated with working with human tissues. This is a vital step forward that will help progress many of our different research programmes.

Our support staff and services have had to constantly adapt and develop over the years to match the growth in our research programmes. That they have been able to do this and consistently maintain a first class research environment is testament to both their dedication and expertise.



Immunoglycomics Group Leaders Dr Mattie Timmer (VUW) and Dr Bridget Stocker

Fundraising

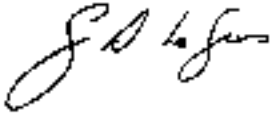
Despite the global recession and its impact on the lives of New Zealanders, public support for the Malaghan Institute has remained constant. This speaks volumes about our wonderful supporters and their commitment to our cause. My sincere personal thanks go out to all those who have contributed towards our efforts in any way, be it financial support or through giving their time. Of particular note are the late Wade Thompson, Kevin Hall, the Wallace Family and the Taylor Family, for their support of some of our most critical research areas. We remain, as ever, aware of the trust placed in us and this awareness fuels our determination to succeed.

In tough economic times there is more pressure than ever among charities to secure the fundraising dollar. The Malaghan Institute is not, and has no desire to be, a "big name" charity. However, we are endeavouring to make our message heard among the din, as we believe we offer something unique and of great value to New Zealanders. To this end we welcomed Annabel Lush, our Northern Region Co-ordinator, who has been tasked with raising our profile in the Auckland region. In 2009 we were also delighted to witness the formation of a new Friends of the Malaghan group in Taupo. Our thanks go to these new Friends – as well as our other groups in Wellington, Hawke's Bay and Auckland – for their tireless efforts on our behalf. Finally I would like to acknowledge the steadfast support of AMI Insurance – who, for many years now, have been a very generous supporter and tremendous ally in all our endeavours.

The Future

At the beginning of 2010 our Trust Board commissioned an independent panel of experts to undertake a review of the Institute's science activities. This review not only found our work to be of the highest international calibre but also praised our ambition – our commitment to seeking tangible clinical outcomes from our research. This kind of research requires time, patience and an extensive network of clinical and research partners in order to succeed. As well as being a tremendous reinforcement of our work, the independent review supports my own opinion that the Malaghan Institute is now uniquely placed to be able to achieve some vital breakthroughs that will redefine the way we treat diseases.

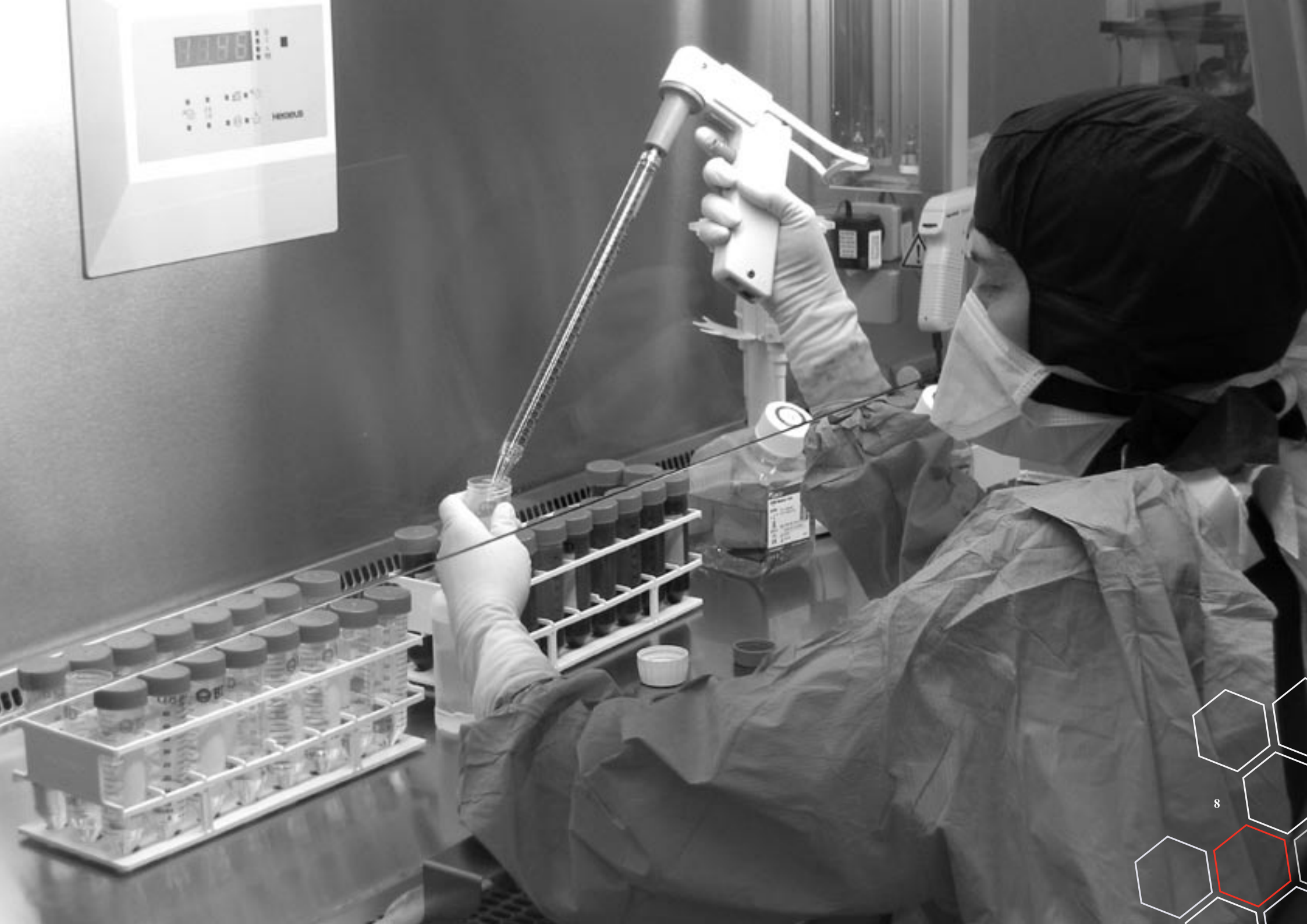
Given our outstanding research staff, our international collaborative links, our exceptional facility and support staff, and our unwavering public support, I believe we are at the beginning of an exciting new stage in our development. It is with both great excitement and great expectation that I look ahead to the next decade of research at the Malaghan Institute.



Prof Graham Le Gros FRSNZ

DIRECTOR

The Hon Tony Ryall (Minister of Health), Faith Taylor, Kathryn Williams and Prof Graham Le Gros at the opening of the Keith and Faith Taylor Cancer Research Laboratories



MALAGHAN INSTITUTE TRUST BOARD

Mr Graham Malaghan *(Chairman) FCILT, PhD honaris causa (VUW)*

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

Mr John Beattie *LLB (VUW)*

Obtained a law degree from Victoria University 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, 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, an Executive Director of the Infinity Investment Group and is the Co-Founder of Genesis Research & Development Corporation Limited.

Prof David Bibby *DSc (Loughborough University)*

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

Assoc Prof John Carter *BMedSc, MBChB(Otago), FRACP, FRCPA*

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

Prof Peter Crampton *MBChB, PhD, FAFPHM, MRNZCGP*

Appointed to the Malaghan Institute Trust Board in 2008. Is 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)*

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

Mr Ray C Kingston

Appointed to the Malaghan Institute Trust Board in June 2009. Until 2008 was Executive Chairman of Link International Group Limited, a company he founded in 1996. With an extensive background in the commercial sector, he has been a Director of many companies in both the private and public sector. Currently serves as Chairman and Director of a number of private commercial enterprises, and is also a current board member and/or Trustee

of - King's College Auckland, King's College Foundation, General Trust Board of the Anglican Church, First Foundation Capital Trust, and a number of other related community organisations.

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

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

Mr Matthew Malaghan *BCom, 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 Chartered Institute of Logistics and the NZ Institute of Directors.

Mr David Mossman *BVSc, MRCVS, MNZIF*

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

Mr Gary Quirke *BCA, CA, FCILT*

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

Dr Jim Watson *PhD (Auckland)*

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

Mr C Dan Williams *CA*

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

MALAGHAN INSTITUTE RESEARCH GROUPS

Arthritis & Inflammation

Group Leader: Dr Jacquie Harper

Group Members: Dr Rebecca Grainger (to Jul 09), Henry Hudson (to Jan 09), Aidan Leong (to Nov 09), Tommy Liu (to Dec 09), Dr Willy-John Martin, Rene McLaughlin, Odette Shaw, Clare Slaney (to Feb 10), Stefanie Steiger, Aras Toker (to Apr 09), Dr Mischa Walton (to Mar 10)

Goal: To improve the management of inflammatory diseases such as arthritis

How: By understanding the onset, duration and resolution of inflammation and identifying new therapies for controlling inflammation

Research Projects:

Research Grants *· Arthritis New Zealand · Foundation for Research, Science & Technology · Health Research Council of New Zealand · New Zealand Lottery Health Research · Nikau Foundation · Wellington Medical Research Foundation*

Asthma & Allergic Diseases

Group Leader: Prof Graham Le Gros

Group Members: Mali Camberis, Dr Elizabeth Forbes-Blom, Dr Marina Harvie, Rachel Hunter (to Dec 09), Helen Mearns, Catherine Plunkett, Melanie Prout, Marcus Robinson, Shiau-Choot Tang, Sarrabeth Stone (to Jan 09)

Goal: To develop vaccines against allergy, asthma and human hookworm

How: By gaining detailed knowledge of the Th2 immune response and applying this information to the design of vaccines

Research Projects:

Research Grants *· AgResearch Ltd Hamilton · Fonterra Co-operative Group Ltd · Foundation for Research, Science & Technology · Harry & Beverley Romanes · Health Research Council of New Zealand · Marjorie Barclay Trust · Maurice Wilkins Centre · New Zealand Lottery Health Research · Rex & Betty Coker Scholarship · The Royal Society of New Zealand Marsden Fund · Wellington Medical Research Foundation*

Cancer Cell & Molecular Biology

Group Leader: Prof Mike Berridge

Group Members: Dr James Baty, Kate Broadley (to Dec 09), Alanna Cameron (to Feb 10), Carole Grasso, Dr Heli Matilainen, Dr Melanie McConnell (to Dec 09), Taryn Osmond (to Dec 09), An Tan, Ching-Wen Tang

Goal: To develop effective cancer treatments that target self-renewing cancer stem cells

How: By using cancer stem cell models to identify novel drug targets and by evaluating the potential of using immunotherapy to eradicate self-renewing cancer stem cells

Research Projects:

Research Grants · *Breast Cancer Research Trust · Cancer Society of New Zealand · Child Health Research Foundation · Genesis Oncology Trust · Melanoma Research Alliance · New Zealand LAM Trust/ LAM Australasia Research Alliance · The Royal Society of New Zealand Marsden Fund · Wellington Medical Research Foundation*

Cell Survival

Group Leader: Dr Melanie McConnell

Group Members: Kate Broadley, Susanna Brow, Carole Grasso, Dr Patries Herst, Dr Heli Matilainen, Taryn Osmond (to Feb 10)

Goal: To identify and understand the mechanisms of cancer cell survival

How: By understanding the basic biology of cancer cells that survive stress and applying that knowledge to the development of new treatment strategies

Research Projects:

Research Grants · *Breast Cancer Research Trust · Cancer Society of New Zealand · Melanoma Research Alliance · Motor Neurone Disease Association of New Zealand · New Zealand Lottery Health Research · Roy McKenzie Medical Research Fellowship · The estates of Ellen, Sinclair, Barbara and Alison Wallace · Wellington Medical Research Foundation*

Immune Cell Biology

Group Leader: Prof Franca Ronchese

Group Members: Dr Haley Ataera (to May 10), Dr Noriyuki Enomoto (to Oct 09), Evelyn Hyde, Sabine Kuhn, Sonai Lim, Joel Zhi-long Ma, Marie Petrie-Deely, Dr Helen Simkins (to Jan 10), Dr Robert Weinkove, Dr Jianping Yang

Goal: To use the immune system to fight disease

How: By gaining a greater understanding of the basic biology of dendritic cells and how they initiate and maintain immune responses

Research Projects:

Research Grants · *Cancer Society of New Zealand · Cancer Society Wellington Division · Genesis Oncology Trust · Haematology Society of Australia and New Zealand · Health Research Council of New Zealand · Leukaemia and Blood Foundation of New Zealand · Maurice Wilkins Centre · New Zealand Lottery Health Research · The Royal Society of New Zealand Marsden Fund · Victoria University of Wellington · Wellington Medical Research Foundation*

Immunoglycomics

Group Leader: Dr Bridget Stocker

Group Members: Dr Mattie Timmer (Co-Group Leader, VUW), Dr Lynton Baird (to Dec 09), Stephanie Chee, Janice Cheng, Hilary Corkran, Emma Dangerfield, Gregory Haslett, Ashna Khan, Gert-Jan Moggre, Dr Ben Mulchin (to Sep 09), Stefan Munneke, Janelle Sauvageau, Anna Win-Mason

Goal: To understand the role of carbohydrates in immune responses, and to apply this knowledge to the development of more effective therapies for diseases such as asthma, cancer and tuberculosis

How: By synthesising novel glycolipids for testing in target immune response assays and experimental disease models

Research Projects:

Research Grants · *Cancer Society of New Zealand · Health Research Council of New Zealand · Industrial Research Limited · New Zealand Lottery Health Research · Tertiary Education Commission · Victoria University of Wellington · Wellington Medical Research Foundation*

Infectious Diseases

Group Leader: Dr Joanna Kirman

Group Members: Lindsay Ancelet, Clarissa Chandrahasen (to Dec 09), Dr Lisa Connor (to Dec 09), Hannah Kelly, Kelly Prendergast, Fenella Rich, Lisa Shaw

Goal: To reduce the incidence of tuberculosis (Tb) in New Zealand

How: Through the development and implementation of more effective Tb vaccines

Research Projects:

Research Grants *· Cancer Society of New Zealand · Foundation for Research, Science & Technology · Maurice Wilkins Centre · New Zealand Lottery Health Research · The Royal Society of New Zealand Marsden Fund · University of Otago · Wellington Medical Research Foundation*

Multiple Sclerosis Research

Research Associate: Dr Anne La Flamme

** Dr La Flamme's research is undertaken at Victoria University of Wellington*

Goal: To identify new approaches and to develop immunotherapies for the treatment of multiple sclerosis (MS)

How: By gaining a better understanding of the immune components that cause neurological damage during MS, and using this knowledge to develop therapeutic treatments that halt its progression

Research Projects:

Research Grants *· The Great New Zealand Trek Charitable Trust Inc · Neurological Foundation of New Zealand · New Zealand Lottery Health Research · Victoria University of Wellington Research Grant · Wellington Medical Research Foundation*

Vaccine Research

Group Leader: Dr Ian Hermans

Group Members: Evelyn Bauer, Dr Nina Dickgreber (to Jul 09), Kathryn Farrand, Dr Peter Ferguson, John Gibbons, Mr Martin Hunn, Deborah Knight, Sara McKee, Brigitta Mester, Taryn Osmond, Dr Troels Petersen, Dianne Sika-Paotonu, Ching-Wen Tang, Catherine Wood

Goal: To design more effective vaccines against diseases such as cancer

How: By exploiting the activity of Natural Killer T cells (NKT cells) to improve vaccine induced T cell responses

Research Projects:

Research Grants · *Cancer Society of New Zealand · Cancer Society Wellington Division · Foundation for Research Science & Technology · Health Research Council of New Zealand · Industrial Research Limited · Maurice Wilkins Centre · New Zealand Lottery Health Research · New Zealand Neurological Foundation · Robert McClelland Trust · Royal Australasian College of Surgeons · Surgical Research Trust · The Graham Hall Bequest · The Royal Society of New Zealand Marsden Fund · University of Otago · Wade Thompson · Wellington Medical Research Foundation*

CANCER

Cancer is a disease that has afflicted people throughout recorded history and is the leading cause of death in New Zealand

Cancer develops when a cell in the body begins to grow out of control. Normally cells grow, divide and die in an orderly fashion, in response to signals from their environment. In cancer cells however, these cues are lost due to genetic defects and the cells continue to grow and divide in an uncontrolled manner. In a process termed metastasis, these abnormal cells can spread throughout the body via the bloodstream or lymph vessels, where they continue to grow and replace normal tissue.

It is a sobering fact that despite decades of research and billions of dollars of funding, cancer death rates have changed little over the past 50 years. What's more, cancer remissions are often transient, drug resistance is a major problem and drug withdrawal can result in an aggressive return of the disease. New, more effective cancer therapies are needed urgently if we are to turn these statistics around.

CANCER PROJECTS

Overview

Immunotherapy holds great promise for the treatment of cancer. The immune system has all the properties that are required to complement existing cancer treatments - immune cells are specific and have the capacity to discriminate between normal and cancer cells; they have powerful effector capacity and can recruit inflammatory cells to destroy neoplastic tissue; they can also migrate to different tissues and eliminate residual disease.

Given the physiological role of dendritic cells in the initiation of immune responses, they are frequently used as adjuvants in immunotherapies such as cancer vaccines. However, while these therapies have shown some promising results, their success remains limited to a minority of patients. Over half of the scientists at the Malaghan Institute of Medical Research are involved in research programmes designed to release the full potential of cancer immunotherapy and the projects are summarised in this section.

Recently there has been a new focus on the cancer stem cell, or tumour initiating cell, and the identification of ways to target immunotherapies against these drug and radiation resistant cancer cells. Like the stem cells that shape the development, repair and replacement of various tissues and organs in our body, cancer stem cells have the unique property of self-renewal and can divide indefinitely. By learning more about the basic biology of cancer stem cells and the pathways they use to survive chemotherapy and radiotherapy treatments, Malaghan Institute scientists hope to develop safe and effective ways to eradicate them.

Over the past decade the Malaghan Institute has progressed its basic biomedical research outcomes into real results for patients - a ‘bench to bedside’ philosophy that has led to three clinical trials including the current phase I glioblastoma multiforme trial. This work is supported by a close working relationship with clinicians from the Wellington Blood and Cancer Centre, and Wellington Hospital, and access to the Institute’s new state-of-the-art GMP vaccine production facility.

By combining the disciplines of immunology, cell biology and drug discovery in a programme that involves immunologists, biochemists, molecular biologists, chemists and clinicians, this research has the potential to launch a new era in cancer treatment.

Using dendritic cell vaccines in the clinic

Contributors: Mr Martin Hunn, Evelyn Bauer, Catherine Wood, Dr Ian Hermans, collaborating with Dr David Hamilton, Marina Dzhelali (CCDHB) and Prof Michael Findlay (CTNZ)

In late 2008 the Malaghan Institute initiated a Phase I clinical trial in collaboration with the Capital & Coast District Health Board to test the feasibility and safety of using dendritic cell vaccines in combination with temozolomide chemotherapy for the treatment of patients with recurrent glioblastoma multiforme, a highly aggressive brain tumour with a 100% fatality rate. This trial is ongoing and open to patients with recurrent glioblastoma multiforme being treated at Wellington Hospital.

Personalised vaccines, such as those being used in the glioblastoma multiforme clinical 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. Complementing the clinical trials is an extensive basic immunology research programme involving several of the Institute's research groups, aimed at understanding anti-tumour immune responses and how they can be more effectively elicited with vaccines.

Making an optimal dendritic cell vaccine

Contributors: Sonai Lim, Joel Zhi-Iong Ma, Sabine Kuhn, Evelyn Hyde, Dr Jianping Yang, Prof Franca Ronchese

Prof Franca Ronchese's Immune Cell Biology Group has shown that dendritic cells can form the basis of effective tumour vaccines. A major focus of their current research is finding ways to improve their efficacy. Dendritic cells can be generated in culture using different growth factors. These *in vitro* generated cells resemble dendritic cells that are found in the body under normal conditions or during inflammation. These two types of *in vitro* generated dendritic cells differ in their ability to respond to different stimuli and to activate immune responses *in vitro*. They are now being used as vaccines to compare their ability to initiate anti-tumour immune responses.

Prof Ronchese's group also found that once injected, the dendritic cells in a vaccine can be attacked and killed, as if the immune system were mistaking them for tumour cells. Surprisingly, they also showed that the consequences of dendritic cell killing are dependent on how the cells have been loaded with tumour antigen, and that the cell's ability to activate immune responses may not be affected. This information will guide the development of dendritic cell vaccines that better stimulate immune responses and minimise the effects of dendritic cell killing.

Defining the characteristics of effective anti-tumour T cells

Contributors: Dr Jianping Yang, Marie Petrie-Deely, Prof Franca Ronchese, collaborating with Dr Pisana Rawson, Dr Bill Jordan & Dr Lifeng Peng (VUW)

The Immune Cell Biology Group have used populations of mouse CD8+ T cells activated in culture to study the properties of effective anti-tumour T cells. They found that CD8+ T cells activated in the appropriate conditions, and injected into mice, are able to reject tumours immediately and maintain their anti-tumour activity for weeks or months. Surprisingly, small changes to the conditions used to activate these CD8+ T cells resulted in a substantial decrease in their ability to reject tumours.

The group are now collaborating with proteomic specialists from the Centre for Biodiscovery (VUW) in order to identify proteins expressed by these cells that are the basis of their differential anti-tumour activity. The functions of lead proteins identified in the proteomic screens are currently being determined.

The knowledge gained from this work will be highly beneficial for guiding the development of vaccination strategies that generate effective anti-tumour T cells.

The role of langerin+ CD8+ dendritic cells in generating T cell mediated anti-tumour immune responses

Contributors: John Gibbons, Dr Ian Hermans, Dr Troels Petersen

While it has long been recognised that dendritic cells are particularly potent immunostimulatory cells, and their role in generating T cell mediated immune responses is critical, it is also evident that many discrete dendritic cell subsets exist.

Recent studies by the Vaccine Research Group have shown that cellular material from injected dendritic cells is acquired by lymphoid resident dendritic cells. In particular it is the langerin+ CD8+ dendritic cells that appear to play a pivotal role in inducing protective CD8+ T cell immune responses to tumours in the blood.

The targeting of vaccine antigens and adjuvant to this dendritic cell subpopulation is therefore an attractive approach for improved dendritic cell immunisation strategies. Considerable effort is now being directed towards understanding the basic biology of langerin+ CD8+ dendritic cells, as well as their role in initiating and maintaining immune responses in blood-borne tumour disease models.

Using natural adjuvants to stimulate the anti-tumour immune response

Contributors: Sabine Kuhn, Fenella Rich, Evelyn Hyde, Dr Jacquie Harper, Dr Joanna Kirman, Prof Franca Ronchese

Dendritic cells found in tumours are often loaded with tumour antigen but not sufficiently activated to initiate an effective anti-tumour immune response. Scientists at the Malaghan Institute are therefore investigating the ability of various stimuli to re-programme tumour-resident dendritic cells, monocytes and macrophages to a more immunostimulatory phenotype. The natural adjuvants *Mycobacterium bovis* BCG, *Mycobacterium smegmatis*, and other 'danger signal' products of infectious and non-infectious origin were injected peri-tumourally and the resulting immune responses analysed.

Interestingly, some of the adjuvants were shown to delay tumour growth and prolong survival. In addition, some adjuvants induced activation of dendritic cells in culture and cytokine secretion. Surprisingly, the effects on dendritic cells and tumour growth did not always correlate, suggesting that other immune cells are probably necessary for the response. Nonetheless, these results suggest that natural adjuvants might eventually become the basis of safe and simple methods to activate the immune system against tumours.

Small molecules for cancer therapy

Contributors: Dr Ben Mulchin, Emma Dangerfield, Janice Cheng, Stephanie Chee, Dr James Baty, Dr Jacquie Harper, Prof Mike Berridge, Dr Ian Hermans, Dr Mattie Timmer, Dr Bridget Stocker

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. The addition of certain glycolipids, 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. The Institute's Immunoglycomics Group, led by Dr Bridget Stocker and Dr Mattie Timmer (VUW) are currently synthesising a variety of novel glycolipids to enhance immunity to tumours. They have also generated fluorescently labelled glycolipids to investigate where they move in the body.

In addition, the Immunoglycomics group has been working towards the development of novel quinolinequinones as cancer drugs. Their efforts have proven fruitful with the identification of several lead compounds that show selective anti-cancer activities.

Improving vaccines with compounds that stimulate NKT cells

Contributors: Dr Troels Petersen, Dianne Sika-Paotonu, Deborah Knight, Sara McKee, Dr Bridget Stocker, Dr Ian Hermans, collaborating with Dr Gavin Painter (IRL, Wellington), Dr Sarah Young & Dr Margaret Baird (University of Otago) and Dr Gill Webster (Innate Therapeutics Ltd, Auckland)

Dr Ian Hermans' Vaccine Research Group has shown that they can generate very strong anti-tumour immune responses when the dendritic cell vaccine is used in combination with the glycolipid α-galactosylceramide (α-GalCer), which stimulates potent anti-tumour immune responses through activation of Natural Killer T (NKT) cells. These results complement their earlier discovery that certain combinations of Toll-like receptor ligands improve dendritic cell activity and will be taken into consideration when formulating clinical vaccine protocols.

Dr Hermans is currently working with Dr Gavin Painter from Industrial Research Limited to determine if they can identify novel glycolipids from bacteria with NKT stimulating activity.

The Vaccine Research Group is also investigating the effects of incorporating NKT cell ligands into vaccines based on virus-like particles in collaboration with Dr Sarah Young, and in bacterial nanoparticles with Dr Gill Webster.

Harnessing NKT cells to treat chronic lymphocytic leukaemia

Contributors: Dr Robert Weinkove, Dr Ian Hermans, Prof Franca Ronchese, collaborating with Assoc Prof John Carter (Wellington Blood & Cancer Centre)

In December 2007 haematologist Dr Robert Weinkove launched the Malaghan Institute's first clinical study into chronic lymphocytic leukaemia (CLL), the most common blood cancer in New Zealand.

Working in conjunction with the Wellington Blood and Cancer Centre, Dr Weinkove is comparing the immune systems of patients with CLL with those of healthy volunteers.

The focus of this study is the NKT cells, which Dr Weinkove believes could be used to improve responses to cancer vaccination.

Dr Weinkove is looking at the function of NKT cells in patients with CLL. He plans to use NKT cells to augment the function of dendritic cells, with a view to developing novel immunotherapies for this condition.

Monitoring dendritic cell vaccines & detecting developing tumours with a novel MRI contrast agent

Contributors: Dr Peter Ferguson, Dr Ian Hermans, collaborating with Angela Slocombe (Wellington Hospital) and Dr Richard Tilley (VUW)

One of the hurdles in clinical vaccine development is the difficulty in monitoring the immune response following vaccination. Furthermore, early diagnosis of cancer could improve the outcome for a large number of patients.

A novel synthesis process to produce superparamagnetic nanoparticles has been developed and patented by Dr Richard Tilley and colleagues at Victoria University of Wellington. The goal of Malaghan Institute Clinical Research Fellow Dr Peter Ferguson is to translate the superior magnetic properties of the nanoparticles into contrast agents that enhance the ability of Magnetic Resonance Imaging (MRI) to test the immunogenicity of dendritic cell vaccines and to detect developing cancers.

The increased contrast provided by the nanoparticles increases the utility of MRI as a non-invasive way of 'seeing' what is happening inside the human body and directly feeds into the Institute's cancer immunotherapy programmes.

Isolation and characterisation of GBM cancer stem cells

Contributors: Kate Broadley, Kathryn Farrand, Mr Martin Hunn, Dr Patries Herst, Dr Ian Hermans, Dr Melanie McConnell

Cancer cells grow under conditions of metabolic and energetic stress. During chemotherapy and radiotherapy treatments of cancer patients, these cells are subjected to further stress, yet some are able to survive and go on to cause relapse and metastasis. This is thought to be due to the presence of cancer stem cells, which are drug and radiation resistant. Dr Melanie McConnell's Cell Survival Group has established various methodologies to allow identification of cancer stem cells and to characterise their function. They are using different cancer models to study the different properties of cancer stem cells – self-renewal and resistance to radiation and chemotherapy using glioblastoma multiforme (GBM) cells; drug resistance in melanoma cells; and metastasis using breast cancer cells.

They have used stem cell culture, stem cell gene markers and drug resistance to identify a population of cells in GBM tumours that are highly tumourigenic and potentially immune suppressive. Neurosurgeon and Malaghan Clinical Research Fellow Mr Martin Hunn has shown that these cells can be recognised by the immune system and protect against tumour development.

Using dendritic cell immunisation to sensitise malignant glioma to chemotherapy

Contributors: Mr Martin Hunn, Kathryn Farrand, Kate Broadley, Dr Melanie McConnell, Dr Ian Hermans

One of the long term aims of the Vaccine Research Group is to develop effective and safe immunotherapies for high grade glioma (brain cancer). Complementing the phase I GBM clinical trial is a basic research programme involving Mr Martin Hunn that is investigating the possibility of directing anti-tumour immune responses specifically against GBM.

Current work is focused on developing a murine model of glioma in which to assess the efficacy and safety of vaccination strategies directed at drug-resistant tumour stem cells, to support the translation of this novel immunotherapy into clinical trial. Mr Hunn has shown that the GBM cells can grow as detached 'neurospheres' in appropriate culture media and that these spheres show increased expression of stem cell-related genes and initiate tumours earlier compared to parental tumour cells. Mr Hunn will also undertake an *in vitro* assessment of the immune responses of patients with recurrent GBM who are being treated with the dendritic cell vaccine in the phase I clinical trial.

Activating the immune system against childhood brain cancers

Contributors: Carole Grasso, Mr Martin Hunn, Dr Ian Hermans, Prof Mike Berridge

The overall goal of this research project, supported by the Child Health Research Foundation, is to apply the Institute's broad knowledge in dendritic cell immunotherapy to the treatment of childhood brain cancers, in particular the brain metastasis associated with childhood leukaemia.

To address this goal, orthotopic models of brain cancer have been established in mice including WEHI-3 myelomonocytic leukaemia, GL261 glioblastoma and EL4 thymoma.

In these models GL261 grow as clearly marginated brain tumours when injected into the cerebral cortex whereas EL4 and WEHI-3 grow as diffuse tumours with poorly defined margins. Significant progress has been made investigating dendritic cell immunotherapy with GL261 tumours grown subcutaneously, but the time-consuming nature of the orthotopic brain tumour model has restricted the number of experiments that have been conducted with this model. Nevertheless, information from GL261 and other subcutaneous tumour models will be applied to the orthotopic brain models in future experiments.

Immunotherapeutic targeting of melanoma stem cells

Contributors: Carole Grasso, Kate Broadley, Prof Mike Berridge, Dr Melanie McConnell, collaborating with Prof Jonathan Cebon (Ludwig Institute, Australia)

As part of a Melanoma Research Alliance-funded collaborative international programme aimed at using immunotherapy to target melanoma stem cells, Prof Mike Berridge, Dr Melanie McConnell and colleagues have explored the role of the putative tumour stem cell surface marker, CD133, in defining tumour-initiating (stem-like) cells in primary human metastatic melanomas.

The tumour-forming capabilities of two distinct populations of malignant melanoma cells, CD133+ and CD133-, were determined by serial passage in NOD/SCID immunocompromised mice. Unexpectedly both populations of cells were shown to initiate and sustain tumour growth with similar frequency, suggesting that CD133 is not a defining marker of stem cells for human malignant melanoma. CD133 negative cells were shown to express CD133 mRNA and intracellular protein, suggesting a failure of exocytosis independent of tumour-forming ability.

Current research is focused on searching for other potential melanoma stem cell markers.

Unleashing the power of the immune system on metastatic breast cancer

Contributors: Dr Melanie McConnell, Dr Troels Petersen, Dr Heli Matilainen, Ching-Wen Tang, Prof Mike Berridge

The Malaghan Institute's breast cancer programme, supported by BCRT, aims to develop functional vaccination strategies that induce a patient's immune cells to seek out and destroy the cells responsible for the initiation and spread of tumours. During the first year of this project a preclinical model of metastatic breast cancer has been established.

Research has also been undertaken to investigate the tumour-forming ability of cells grown under conditions that generate tumourspheres, cell clusters that in other tumour models exhibit cancer stem cell-like properties. Surprisingly, cells from breast cancer tumourspheres did not express stem cell-like gene expression markers and did not produce more aggressive tumours. Furthermore, cells from tumourspheres showed lower lung metastases, suggesting they are not stem cell-like.

This led researchers to focus on the metastatic cells in the lungs of tumour-bearing mice and to use these cells in vaccination approaches. An important outcome of this work has been the demonstration that breast cancer cells are immunogenic and generation of immune responses can protect against tumour growth and metastasis.

Metabolic constraints on tumour metastasis

Contributors: Alanna Cameron, An Tan, Prof Mike Berridge collaborating with Francesco Vieceli Dalla Sega (University of Bologna, Italy)

Whereas tumour cells and other rapidly-dividing cells in the body primarily use glycolytic metabolism to fuel their bioenergetic and biosynthetic needs, non-dividing functional cells in muscle and brain are driven by oxygen-dependent mitochondrial energy metabolism. Prof Mike Berridge's Cancer Cell & Molecular Biology Group, with support from Genesis Oncology Trust, has modelled the bioenergetic needs of cancer cells by ablating the mitochondrial genome of a metastatic melanoma, and a breast carcinoma cell line. Tumour growth at the primary site was delayed by 20-30 days and lung tumours failed to form when these cells were injected intravenously.

The anti-diabetic drug metformin has been associated with a reduced incidence of breast cancer and has also shown suppressive effects in colorectal and lung cancer. Prof Berridge and colleagues went on to show that metformin, and the heterocyclic polyketide mycothiazole, fail to inhibit cell growth responses in mitochondrial gene knockout tumour cells. These results raise the possibility of using these drugs to sensitise tumour cells to glycolytic inhibitors in cancer treatment.

Sirtuins, stress and survival: A problem in anti-tumour therapy

Contributors: Susanna Brow, Kate Broadley, Dr Patries Herst, Dr Melanie McConnell

A fundamental aspect of cancer cell survival is the ability of cancer cells to change the metabolic pathways to cope with cellular stress. Understanding the survival mechanisms is key to designing effective anti-tumour therapeutics. The sirtuin family (SIRT1-SIRT7) are NAD+-dependent enzymes with deacetylase activity, ADP-ribosyl transferase activity, or both. Based on NAD+-dependence, SIRT1 in particular has been postulated to be a metabolic sensor, relaying information on the metabolic status of the cell to the regulators of gene expression.

SIRT1 inhibition has the potential to bring specificity to cancer treatment, if in fact normal cells are less reliant on SIRT1-mediated survival pathways. In particular, where a conventional approach such as chemotherapy causes a stress response and induces survival pathways in the target cell, combining SIRT1 inhibition with that approach will potentially allow greater efficacy of cancer cell drug targeting. The Cell Survival Group is investigating whether SIRT1 inhibition reduces cancer cell survival when combined with cytotoxic drugs, radiation or oxidative stress.

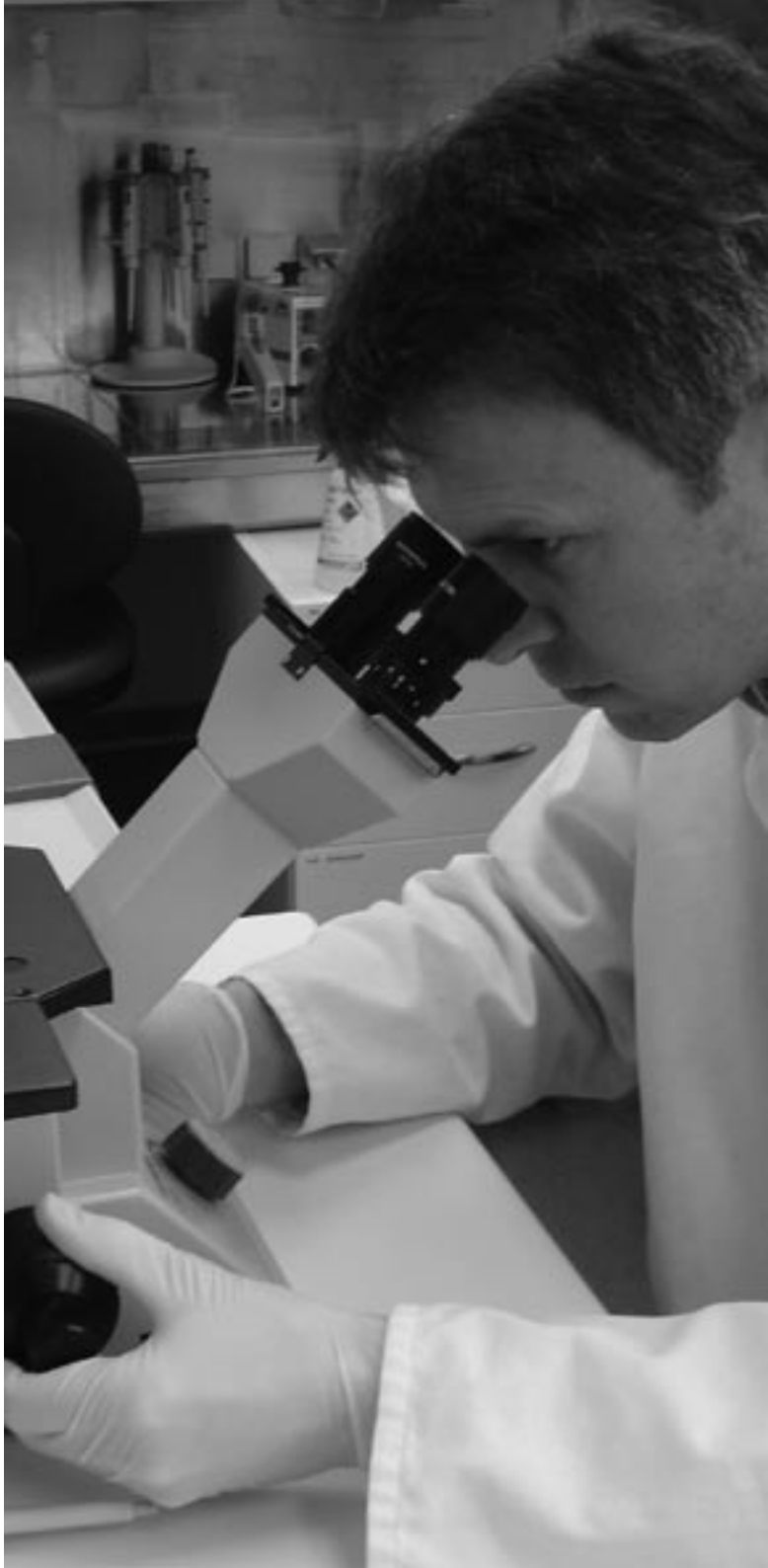
Self renewal properties of LAM cells

Contributors: Dr James Baty, Prof Mike Berridge, collaborating with Prof Judy Black & Dr Lyn Moir (Woolcock Institute, Sydney, Australia)

Lymphangioleiomyomatosis (LAM) is a progressive cellular disease characterised by excessive smooth muscle-like cells in the lungs of young women in their childbearing years. LAM cells have cancer cell-like properties, including mutations in tumour-suppressor genes, loss of cell growth control and abnormal differentiation, and there is evidence for LAM cell metastasis from lung tissue.

An early focus of Dr James Baty's research, supported by NZ LAM Trust/LAM Australasia Research Alliance, has been to determine whether airway smooth muscle cells from LAM patients express stem cell-like self-renewal properties when grown in serum-free medium. Dr Baty has shown that cells from both LAM and non-LAM patients survive but do not proliferate under these conditions, and that they up-regulate some self-renewal genes but not others. Thus self-renewal gene expression does not distinguish LAM cells from non-LAM cells.

The ultimate goal of this research is to develop effective immunotherapies for LAM patients.



ASTHMA & ALLERGY

Asthma, eczema, and food allergies are becoming increasingly common in developed countries and are now recognised as a major global health issue

Allergic diseases such as asthma, food allergy, eczema and allergic rhinitis (including hay fever) are caused by an overreaction of the immune system to harmless environmental triggers. In fact it is only one part of the immune system that seems to be activated – the so-called Th2 immune response that normally functions in protecting against parasitic worm infections.

Asthma is the world's most common chronic disease in children and its prevalence in New Zealand is amongst the highest in the world, affecting approximately 20% of 6 to 14 year olds. Food allergies are also on the rise, particularly amongst children, and in serious cases can lead to food-induced anaphylaxis and death. In developed countries, around 10 to 20% of children will experience eczema at some point during childhood, with the majority of cases occurring before the age of five.

ASTHMA & ALLERGY PROJECTS

Overview

The treatment of immune-mediated diseases of excessive immune activation, such as asthma and allergy, usually involves the use of non-specific immune suppressive agents such as corticosteroids. Although effective at inhibiting the undesired immune response to allergens, these treatments are non-specific in their mechanism of action and can leave patients more susceptible to common infections such as influenza.

Understanding the signals that trigger the initiation of allergic responses is critical for the identification of specific treatments that selectively suppress only the allergic immune response. Surprisingly, little is known about these signals but scientists at the Malaghan Institute hope to change this by using allergic murine models, immunological assays and structure/function analyses to generate much needed information in this poorly understood field.

Important outcomes of this work will be the development of generally applicable vaccines and therapies for the treatment of individuals with established disease, and the identification of improved immunological markers for monitoring human airway inflammation and allergy.

Modelling the Th2 immune response

Contributors: Mali Camberis, Dr Elizabeth Forbes-Blom, Dr Marina Harvie, Helen Mearns, Catherine Plunkett, Melanie Prout, Marcus Robinson, Shiau-Choot Tang, Sarrabeth Stone, Prof Graham Le Gros

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 this question Prof Graham Le Gros' Asthma & Allergic Diseases Group have developed a novel model using GFP reporter mice to look at the early events of Th2 sensitisation in response to common allergens such as house dust mites, pet dander, cockroaches, peanuts and nematode worms.

Prof Le Gros' research team are also using a multi-disciplinary approach to tackle the intriguing question of what makes an allergen an allergen.

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

The basic biology of the Th2 immune response

Contributors: Helen Mearns, Dr Marina Harvie, Melanie Prout, Shiau-Choot Tang, Prof Graham Le Gros, collaborating with Assoc Prof Booki Min & Dr William Paul (NIH, USA) and Dr Melanie Kleinshek (SP Biopharma USA)

A greater knowledge of the basic biology of the Th2 immune response is required in order to develop effective therapies for the treatment of allergic disease. Research from Prof Graham Le Gros' Asthma & Allergic Diseases Group demonstrated that *in vivo* differentiation of naïve CD4 T cells to Th2 status can occur independently of IL-4 and STAT-6 signalling – highlighting an as yet undefined alternative pathway for Th2 differentiation.

The cytokine IL-25 has shown itself to be a particularly interesting target because of its ability to amplify allergic immune responses in both murine models and human disease. By combining IL-25 deficient mice with a GFP based Th2 reporter assay, Prof Le Gros hopes to create a novel tool that can be used to determine the specific biological roles that IL-25 plays in Th2 development in the context of allergic airway disease. The effect of innate signals commonly associated with the 'natural' allergen challenge on IL-25-dependent induced allergic responses will also be determined.

Getting to the guts of allergic inflammation

Contributors: Dr Elizabeth Forbes-Blom, Mali Camberis, Melanie Prout, Shiau-Choot Tang, Catherine Plunkett, Marcus Robinson, Prof Graham Le Gros

Food allergy and associated anaphylaxis have emerged as very significant public health problems, particularly in children. The onset of food allergy is often preceded by atopic dermatitis, commonly known as eczema, leading Prof Graham Le Gros and Dr Elizabeth Forbes-Blom to hypothesise that individuals with food allergy might become sensitised to food allergens by routes other than the gastrointestinal tract.

One such route is via the skin, a unique organ that is exposed to different allergens on a daily basis and interfaces with the immune system. To identify the key cellular and molecular events responsible for the elicitation of food-induced allergic responses, Dr Forbes-Blom has developed a physiologically relevant murine model of skin sensitisation for testing food allergens such as peanut and egg. It is also being used to determine the effect of early childhood Staphylococcal skin infections on the development of food allergy.

Anti-allergy effects of dairy ingredients

Contributors: Mali Camberis, Dr Elizabeth Forbes-Blom, Catherine Plunkett, Melanie Prout, Marcus Robinson, Prof Graham Le Gros, collaborating with Dr James Dekker, Dr Neill Haggarty & Dr Alastair MacGibbon (Fonterra)

Several studies have found that infants from families consuming unpasteurised (or 'raw') cows' milk have much lower rates of allergic disease. However, raw milk cannot be used as a consumer product for food safety reasons, and identification of the anti-allergy factor is difficult due to the complex make-up of raw milk.

In a new project that combines the immunology research strengths of the Malaghan Institute with the dairy science and food safety capabilities of Fonterra, the anti-allergy component present in raw milk is being investigated using newly developed murine models of allergic sensitisation.

The goal of this work is to isolate and develop a functional food-safe ingredient that is able to prevent the onset of allergic disease in humans.

Defining the immunomodulatory properties of milk

Contributors: Marcus Robinson, Dr Elizabeth Forbes-Blom, Mali Camberis, Melanie Prout Prof Graham Le Gros, collaborating with Dr Ali Hodgkinson (AgResearch, Hamilton)

In other research the imunomodulatory properties of goats milk are being examined.

The goal of this project is to define the factors that contribute to milk allergy and to apply this knowledge to the development of an allergy-friendly infant formula.

By understanding the complex interactions between the gut and the host immune system, Prof Le Gros' research team, in collaboration with Dr Ali Hodgkinson from AgResearch, hope to further our understanding of how the immune system responds to milk and what components of milk contribute to the development of allergy.

The effect of berry fruit on lung inflammation

Contributors: Odette Shaw, Dr Mischa Walton, Dr Jacquie Harper, collaborating with Dr Roger Hurst (Plant & Food Research)

Dr Jacquie Harper and colleagues have been involved in an ongoing collaboration with Dr Roger Hurst from Plant & Food Research, who has research expertise in health and food.

Using the OVA model of airway inflammation, they have shown that berry fruits have the ability to lower infiltration of damage-causing inflammatory cells in the lung.

This work could lead to the development of anti-inflammatory fruit-based foods for improving the management of inflammatory conditions such as asthma.

A sweet approach to asthma

Contributors: Gert-Jan Moggre, Janelle Sauvageau, Dr Lynton Baird, Gregory Haslett, Prof Graham Le Gros, Dr Mattie Timmer, Dr Bridget Stocker, collaborating with Dr Ian Sims (IRL)

Few studies have looked at the molecular structures of the allergens that trigger asthma 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, Dr Bridget Stocker observed that particular carbohydrate structures were conserved. Interestingly, antigens derived from bacteria and viruses neither possess these carbohydrate structures nor stimulate allergic immune responses, leading her to hypothesise that these unique structural motifs might be responsible for biasing the immune response towards Th2.

To investigate this hypothesis the Immunoglycomics Group is synthesising a library of carbohydrates for testing in Th2 immune response assays, as well as investigating the role that glycolipids from 'gut' bacteria have in the allergic immune response. It is anticipated that these studies will provide the first detailed insight into the relationship between glycoconjugate 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.

CTL-mediated immunotherapy of allergic airway inflammation

Contributors: Dr Noriyuki Enomoto, Evelyn Hyde, Joel Zhi-Iong Ma, Dr Jianping Yang, Prof Graham Le Gros, Prof Franca Ronchese

Dendritic cells play a critical role in allergic airway inflammation through their ability to take up and present allergens and induce local Th2 cell activation and consequent inflammation. Prof Franca Ronchese and colleagues have used a murine model to show that allergen-specific CD8+ cytotoxic T lymphocytes (CTLs) can ameliorate allergic airway inflammation, apparently by killing the airway dendritic cells that induce inflammation.

They are now extending this work by examining how populations of dendritic cells in the airway and lymph nodes are affected by CTL treatment and how these changes in dendritic cell populations may in turn affect the activation of airway Th2 cells.

The mechanism of CTL immunotherapy and its effects on airway inflammation and CD4+ T cell memory will be established and compared to steroid treatment, the current therapy for asthma.

The findings from this research will be used to develop allergen-specific treatments of allergic airway disease.

INFLAMMATION & AUTOIMMUNITY

Some diseases, such as gouty arthritis and multiple sclerosis, are the consequence of an overactive immune system

Gout is one of the most painful forms of arthritis and is caused by the build-up of crystals of uric acid (MSU) in the joints. The immune system identifies MSU crystal deposition as a ‘danger signal’. This initiates the rapid inflammatory response responsible for swelling, heat and intense pain in the affected joint. Development of chronic gout can lead to severe joint damage and loss of joint function. The prevalence of gout in New Zealand is twice that observed internationally and it is three times more common in Maori and Pacific populations.

Multiple sclerosis (MS) affects one in every 1,500 New Zealanders, which is one of the highest frequencies of this disease worldwide. 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. Women are almost three times more likely to develop MS than men and, because the disease hits adults in their prime, it dramatically reduces quality of life. No cure has been found and while some treatments are available to help manage the disease, these treatments are not equally effective in all MS patients.

INFLAMMATION & AUTOIMMUNITY PROJECTS

Overview

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

The first approach is to understand the basic biology of inflammatory immune responses, in order to identify potential therapeutic targets or new markers of disease progression. This research is being undertaken using experimental laboratory models and, where possible, in a clinical setting with the involvement of patients.

In conjunction with this work is a separate drug discovery programme aimed at identifying potential therapeutic compounds that can be used to halt disease progression.

Role of macrophages and monocytes in acute gouty arthritis

Contributors: Dr William John Martin, Odette Shaw, Tommy Liu, Stefanie Steiger, Dr Jacquie Harper

The causative agent of gouty arthritis (MSU crystals) is well documented, however the cellular interactions that underpin the initiation and resolution of an acute gout attack remain poorly understood.

The Arthritis & Inflammation Group, led by Dr Jacquie Harper, has made significant progress in this area by studying the immune cells at play during an acute episode of gout. Challenging the previous belief that monocytes differentiate into anti-inflammatory cells that resolve inflammation in an acute attack of gout, Dr Harper's research shows that these cells in fact develop into pro-inflammatory macrophages *in vivo* and are primed to exacerbate inflammation in the presence of ongoing MSU crystal deposition in the joint.

Their research is now focused on determining what processes orchestrate the development of the pro-inflammatory macrophages during the gout inflammatory response.

A clinical study of gouty arthritis

Contributors: Dr Rebecca Grainger, Rene McLaughlin, Dr William John Martin, Dr Jacquie Harper

In 2006 Dr Harper and colleagues launched a clinical study to compare the immune responses of gout patients and asymptomatic individuals with elevated levels of uric acid in the blood (hyperuricaemia – a precursor to gout), with those of healthy subjects when exposed to gout-causing MSU crystals.

Results from the study, which were published in the Journal of Rheumatology in 2010, revealed that neutrophils isolated from gout patients and individuals with hyperuricaemia are 'primed' to respond to gout causing MSU crystals, and release high levels of inflammation-causing agents that contribute to disease onset and severity.

These findings suggest that hyperuricaemia plays an important role in the development of gout. A follow-up clinical study is now underway to investigate what effect lowering blood uric acid levels in gout patients has on inflammatory immune responses to MSU.

The effects of lipoglycan related compounds on inflammatory immune responses

Contributors: Dr William John Martin, Deborah Knight, Odette Shaw, Dr Ian Hermans, Dr Jacquie Harper, collaborating with Dr Phillip Rendle & Dr Gavin Painter (IRL), Assoc Prof Sarah Hook, Prof Thomas Rades & Dr David Larsen (University of Otago) and Prof Bryce Buddle (AgResearch)

In 2008 a multidisciplinary drug discovery initiative was launched in collaboration with Industrial Research Limited, University of Otago and AgResearch, to develop and test novel carbohydrate-lipid based compounds for their potential to either enhance or suppress inflammatory immune responses.

A focus of this programme is the identification of compounds with adjuvant properties that can be used to enhance tumour-specific immune responses for the development of more effective cell-mediated vaccines.

Lipoglycan related compounds are also being evaluated for their potential to suppress inappropriate inflammatory responses such as those seen in asthma and allergy.

Immunomodulatory effects of NZ native honeys

Contributors: Aidan Leong, Dr Patries Herst, Dr Jacquie Harper, in collaboration with Dr Ralf Schlothauer (Comvita NZ Ltd)

Honey has been used as a natural therapy for centuries and recently there has been growing interest in investigating its putative anti-inflammatory properties.

In 2009 a new research project was undertaken at the Malaghan Institute to determine the ability of different New Zealand native honeys to suppress neutrophil-driven inflammation *in vivo* and *in vitro*.

This work revealed that a particular variety of native honey was able to interfere with inflammatory neutrophil function *in vitro* and, when applied topically, could decrease swelling and inflammatory cell infiltration *in vivo*.

These results suggest a potential clinical application for certain New Zealand indigenous honeys in the treatment of acute inflammatory conditions.

A key role for blood monocytes in EAE

Contributors: Dr Clare Slaney, Aras Toker, Dr Anne La Flamme, Assoc Prof Thomas Bäckström, Dr Jacquie Harper, collaborating with Prof John Fraser (The University of Auckland)

Experimental autoimmune encephalomyelitis (EAE) is a well established murine model of multiple sclerosis (MS) that has been used by scientists at the Malaghan Institute to better understand the causes of MS, and to test the therapeutic potential of compounds designed to halt its progression. An important outcome of this work has been the identification of a key role for blood monocytes in maintaining immune tolerance in EAE. The monocytes were shown to suppress inflammatory T cell responses in naive mice but lost this function when EAE was induced.

The MS drug Glatiramer acetate was shown to be taken up by the monocytes and cells exposed to the drug demonstrated increased intrinsic T cell suppressor activity. Similar outcomes were obtained with an immune-modifying superantigen compound developed by Prof John Fraser.

These findings have important clinical implications for the design of novel immunotherapeutic agents that target specific cell types for the treatment of individuals with MS.

Targeting macrophage activation for the treatment of MS

Contributors: Dr Anne La Flamme, Sarrabeth Stone, Delgertsetseg Chuluundorj, Dr Scott Harding (CCDHB) collaborating with Dr Jacquie Orian (La Trobe University)

Macrophages are multifunctional immune cells and are key mediators of inflammatory immune processes. During inflammation the immune 'climate' of an organism shapes the type of immune response that develops and directs immune cells such as macrophages to promote or resolve disease.

Malaghan Institute Research Associate Dr Anne La Flamme and colleagues have shown that treatments that alter a macrophage's state of activation, and thus alter the immune climate, can prevent central nervous system inflammation and progressive paralysis in the murine model of human MS - experimental autoimmune encephalomyelitis (EAE).

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

Investigating immune regulation of microglial function

Contributors: Sarrabeth Stone, Dr Anne La Flamme collaborating with Assoc Prof Bronwen Connor (University of Auckland)

Immune cells including T cells, macrophages, and microglia (brain-resident macrophages) are responsible for the damage to the nerves and subsequent clinical features of MS.

While many current MS treatments target T cells, because microglia are involved in controlling central nervous system inflammation and damage, microglia may also be a valuable target for new therapies.

Dr Anne La Flamme and colleagues are investigating the immune factors that regulate microglia function in the brain using the EAE model of MS, in the hope that targeting these factors will prevent central nervous system inflammation and damage.

Exploiting anti-cancer and immune-modulating drugs for the treatment of MS

Contributors: Marie Kharkrang (VUW), Dr Anne La Flamme, collaborating with Prof John Miller & Assoc Prof Peter Northcote (Victoria University of Wellington) and David O'Sullivan & Assoc Prof Bronwen Connor (The University of Auckland)

Current disease-modifying therapies used to treat individuals with MS have variable efficacy in reducing the neurological and physical disability associated with the disease.

Recently Dr La Flamme's research group have demonstrated that drugs that prevent cellular proliferation, such as those used to treat cancer patients or immune-modulatory drugs that work to suppress immune responses, are also effective at reducing the incidence and severity of MS in experimental disease models.

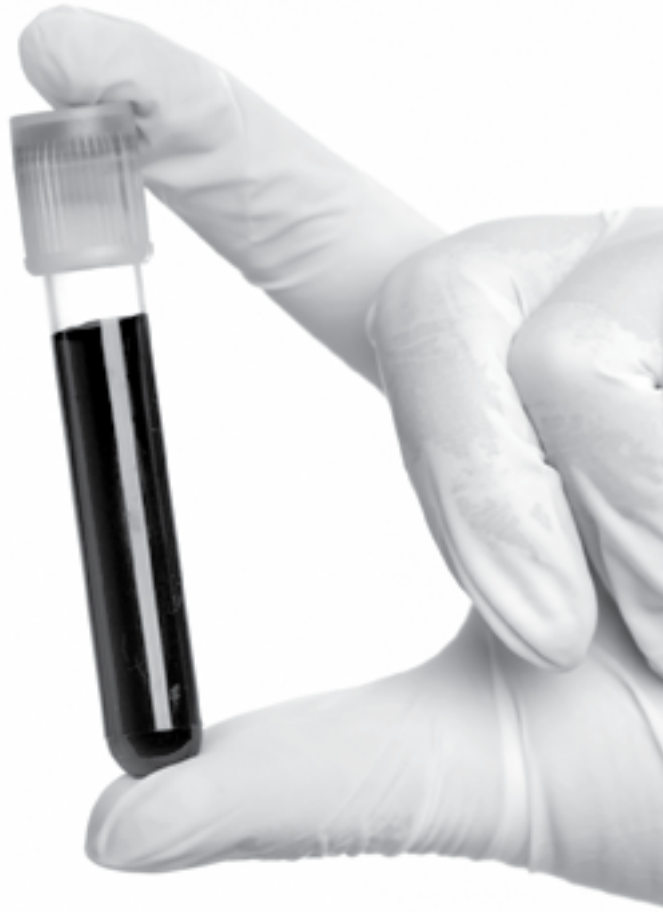
Dr La Flamme is currently investigating the potential of these classes of compounds for treating MS with the hope that the use of drugs that are already in clinical practice, or are in the process of gaining FDA approval for clinical use, will accelerate the path from drug design to clinical application.

INFECTIOUS DISEASES

Tuberculosis kills more people than any other bacterial disease and more than 1 billion people worldwide are infected with hookworm

The World Health Organization (WHO) has considered tuberculosis (Tb) a global emergency for 15 years. Tb claims a staggering 1.7 million lives and newly infects 8.9 million people every year, making it the leading cause of mortality by an infectious disease, after HIV. In New Zealand there are approximately 350 notifications of Tb cases per year.

Hookworm is a leading cause of maternal and child fatalities in developing countries. Once in a host, hookworms suck blood voraciously from the walls of the small intestine causing significant risk of anaemia, a decrease in red blood cells, and loss of iron and protein in the gut. The current approach to controlling hookworm involves frequent use of anthelmintic drugs in school-age children. However, high rates of re-infection occur soon after treatment and there is evidence of emerging drug resistance.



INFECTIOUS DISEASES PROJECTS

Overview

Highly lethal outbreaks of extensively drug resistant tuberculosis (Tb) and evidence of emerging drug resistance in hookworm control, have highlighted the need for more effective therapies to control these diseases.

Dr Joanna Kirman's Infectious Diseases Group and Prof Graham Le Gros' Parasitology team believe the only long-term solution to controlling infectious disease is through vaccination, and are using well established models of Tb and parasite infection in combination with cytokine and cell knockout mouse models to achieve this goal. Complementing this research is a drug discovery platform involving Dr Bridget Stocker's Immunoglycomics Group.

The knowledge and technologies emerging from these research programmes will provide valuable insight into which cytokines and cells need to be targeted both for vaccine design and testing of vaccine efficacy in the field.

This work represents an important New Zealand contribution to the global vaccine initiatives against tuberculosis and human hookworm.

Development of more effective tuberculosis vaccines

Contributors: Hannah Kelly, Fenella Rich, Dr Joanna Kirman, collaborating with Dr Shaun Lott (The University of Auckland)

During an early infection *Mycobacterium tuberculosis*, the causative agent of Tb, grows actively before it enters a dormancy or latency phase in which its growth slows down. Tb is estimated to infect one third of the world's population and in most infected individuals the bacteria are present in the dormant phase.

While the current Tb vaccine Bacille Calmette Guérin (BCG) and other Tb vaccines in clinical trials establish strong immune responses against antigens expressed by actively growing *M. tuberculosis*, until recently the antigens expressed by latent bacilli have been largely ignored.

The antigens produced during the active and dormant growth phases are quite different, so Dr Kirman and colleagues in collaboration with Dr Shaun Lott from The University of Auckland, are seeking to develop vaccines that target multiple Tb antigens. These vaccines are anticipated to work more effectively because any bacilli that escape the initial host response directed against proteins expressed during active growth will subsequently be subject to a memory immune response directed against proteins expressed during dormancy.

The role of langerin+ CD8+ dendritic cells in priming immune responses to BCG

Contributors: Kelly Prendergast, Dr Ian Hermans, Dr Troels Petersen, Dr Joanna Kirman

Considerable effort is now being directed at vaccination strategies that target antigens to dendritic cells with known function.

An interesting subset of dendritic cells expresses the cell surface markers langerin and CD8. This DC subset is found in the marginal zone of the spleen and is thought to play an important role in screening the blood for systemic antigens.

Dr Kirman's Infectious Diseases Group is working with Dr Troels Petersen and colleagues to determine if these cells can prime T cell immune responses against intravenous BCG infection - a model of systemic bacterial infection.

They will also investigate whether langerin+ CD8+ DCs play a role in controlling bacterial BCG burden and reactivating memory T cells.

The outcome of this work will be a greater understanding of the dendritic cell types involved in mediating immunity against mycobacteria.

Characterisation of the CD4+ memory T cell population that protects against Tb

Contributors: Dr Lisa Connor, Lindsay Ancelet, Dr Marina Harvie, Hannah Kelly, Fenella Rich, Prof Graham Le Gros, Dr Joanna Kirman, collaborating with Dr Volker Brinkmann (Novartis, Switzerland)

The BCG vaccine fails to reliably protect against adult Tb lung disease. Efforts to develop a new, more effective vaccine for Tb have been hampered by a lack of understanding of the memory immune response required for protection.

One of the goals of Dr Kirman's Infectious Diseases Group is to understand which of the protective cell types generated after BCG vaccination are important for mediating vaccine-induced protection against Tb. Using the immunomodulatory properties of fingolimod (FTY720), which traps cells in the lymph node, they looked to see whether the lung-resident memory CD4+ T cells generated by BCG vaccination were sufficient to maintain immunity. From these studies they concluded that local memory immune responses are essential for the early control of bacterial growth, thus providing a vital clue regarding which cell types to target for long term protection against Tb.

This work is continuing to characterise the protective lung-resident CD4+ memory population using T cell receptor transgenic models.

Worms and germs

Contributors: Hannah Kelly, Mali Camberis, Fenella Rich, Prof Graham Le Gros, Dr Joanna Kirman, collaborating with Prof Bryce Buddle (AgResearch)

A number of hypotheses have been put forward to account for the observed failure of the BCG vaccine to protect against pulmonary Tb. One of these stems from the observation that countries where BCG is less effective have high parasitic worm burdens, leading to the proposal that worm infections close to the time of vaccination might impair the efficacy of the BCG vaccine. Given that many of the new vaccines in the clinical testing pipeline include BCG as a vaccine component, it is vital to determine how worm infection could influence the ability of the vaccines to protect against Tb.

Using a well characterised murine model of helminth infection, *Nippostrongylus brasiliensis*, Dr Kirman and colleagues found that helminth infection diminished the protective efficacy of BCG vaccination against aerosol infection with *M. tuberculosis* and are currently following up on two leads as to why this occurs.

This knowledge will be used to guide the development of new vaccines against Tb that work in situations where BCG fails.

New drug targets in the fight against *Mycobacterium tuberculosis*

Contributors: Emma Dangerfield, Ashna Khan, Hilary Corkran, Stephanie Chee, Fenella Rich, Dr Joanna Kirman, Dr Mattie Timmer, Dr Bridget Stocker

In view of the problems associated with current Tb treatments, Dr Stocker and colleagues decided to try a different drug discovery approach that targets 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 developed by the Institute's Immunoglycomics Group, which gives high yields while having the added advantage of being better for the environment.

Dr Stocker and colleagues are also developing novel molecular probes, based on cell wall components of *M. tuberculosis* that can be used to elucidate mechanisms underlying the pathogenesis of the disease. Other *M. tuberculosis* cell wall components have also been prepared and are currently being assessed for their immunomodulatory properties.

Novel vaccine approaches for protecting against helminth parasites

Contributors: Mali Camberis, Dr Marina Harvie, Shiau-Choot Tang, Melanie Prout, Rachel Hunter, Prof Graham Le Gros, collaborating with Brett Delahunt (Wellington School of Medicine & Health Sciences) and Dr William Paul (NIH, USA)

Vaccination is currently viewed as the only long-term solution to preventing human hookworm infection. However, the cell types, tissues, effector molecules and cytokines that mediate protective immunity against helminth parasites, and are the key to a good vaccine, remain largely undefined. Previous work from Prof Graham Le Gros' laboratory using knockout models and the rodent hookworm *Nippostrongylus brasiliensis*, identified MHC Class II, STAT6 and IL-4 as important immunological parameters for generating protection in the lung. They are now extending this work by examining the role of basophils in protective immunity using IL-3 knockout models, as well as looking at the involvement of the innate cytokines IL25, RelmA and RelmB.

In a recent study Prof Le Gros and colleagues discovered that the immune cells resident in the lung are critical for establishing protective immunity against tissue migrating hookworm larvae. These findings open novel areas of research in protective immunity against helminth parasites.

NEW AREAS OF RESEARCH AND DEVELOPMENT

Scientists at the Malaghan Institute of Medical Research strive to be at the forefront of innovation and creativity

In this section we profile two new areas of research and development in the fields of Immunoglycomics and motor neurone disease.

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

Motor neurone diseases (MND) are characterised by increasing weakness of the muscles due to the death of the neurons that feed into them. This leads to a progressive and terminal paralysis of the body while leaving the memory and intellect intact. There is currently very little that can be done to slow progression of the disease.

NEW AREAS OF RESEARCH AND DEVELOPMENT PROJECTS

Iminosugars as glycosidase inhibitors

Contributors: Anna Win-Mason, Stefan Munneke, Dr Mattie Timmer, Dr Bridget Stocker, collaborating with Dr Peter Tyler (IRL, Wellington)

Glycosidases are involved in a wide range of important biological processes such as intestinal digestion, posttranslational processing of the sugar chain of glycoproteins, quality-control systems in the endoplasmic reticulum (ER) and the ER-associated degradation mechanism, and the lysosomal catabolism of glycoconjugates.

Inhibition of glycosidases can therefore have profound effects on carbohydrate catabolism in the intestines; maturation, transport, and secretion of glycoproteins; and can alter cell-cell or cell-virus recognition processes. In view of this, glycosidase inhibitors have much potential for the treatment of viral infection, cancer and genetic disorders.

Using their recently developed patented methodology, the Immunoglycomics Group, headed by Dr Bridget Stocker and Dr Mattie Timmer (VUW), has developed rapid and efficient routes towards the preparation of a number of iminosugars, which can function as glycosidase inhibitors. Lead iminosugars identified in this work will be characterised further using various disease models to evaluate their effectiveness as therapeutic drug candidates.

SIRT1 and stress responses in MND

Contributors: Susanna Brow, Dr Melanie McConnell

A new research programme, supported by the Motor Neurone Disease Association of NZ and the estates of Ellen, Sinclair, Barbara and Alison Wallace, has recently been initiated at the Malaghan Institute to identify specific targets of the stress response protein SIRT1 that are relevant to the survival of neurons in individuals with motor neurone disease (MND).

The ability to cope with stress is a fundamental aspect of cell survival. Stresses such as protein misfolding, oxidative stress, inflammation and dysfunctional mitochondrial metabolism occur normally during the aging of a cell, but are abnormally accelerated in MND.

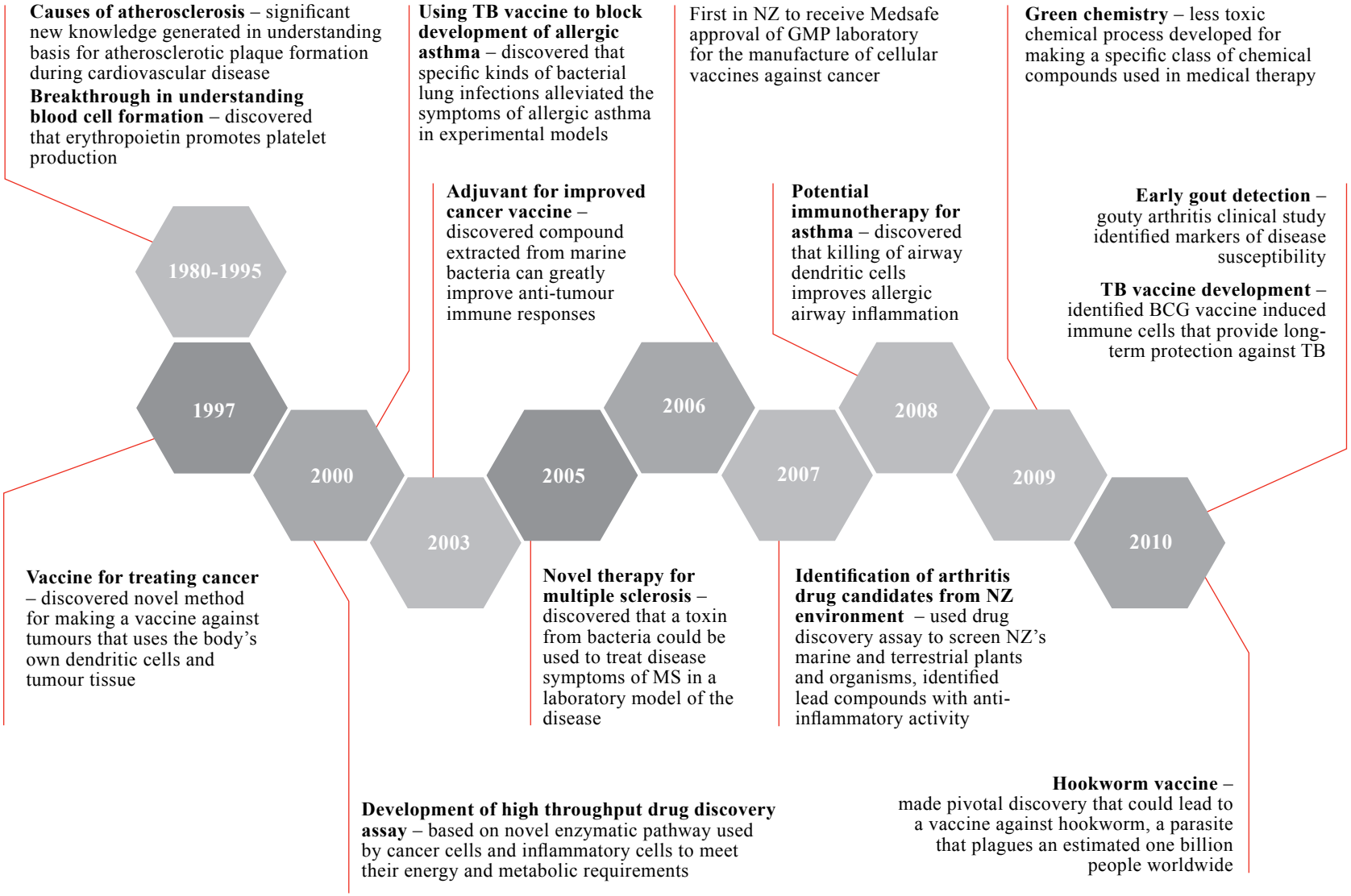
SIRT1 is a key mediator of stress responses and has been shown to be upregulated in neurons. However, little is known about its expression in neighbouring astrocytes, which play a critical role in signalling to neurons to keep them alive.

Dr Melanie McConnell's Cell Survival Group is addressing this question by treating normal astrocyte cells with stresses that induce a MND phenotype, before and after SIRT1 activation.

Careful examination of the precise effects of SIRT1 activation in these cells will aid in the development of approaches to reduce or prevent neurodegeneration.

A HISTORY OF INNOVATION

A timeline of the Malaghan Institute's major achievements in medical research



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Full details of all 'in press' publications will appear in the 2010/11 Annual Report.

SEMINARS

2009

February

Dr Troels Petersen, Malaghan Institute of Medical Research. The role of splenic langerin-positive DCs in cross-presentation of protein & glycolipid antigens

Prof Tony Blakely, Wellington School of Medicine, University of Otago. Tracking Disparity: Ethnic trends in mortality in Aotearoa/NZ 1981 to 2004

March

Dr Kylie Quinn, VRC, NIAID, National Institutes of Health, Bethesda, MD, USA. Influence of CD4+ Th1 cells on the CD8+ response following heterologous prime-boost immunisation

Prof Mark Smyth, Cancer Immunology Programme, Peter MacCallum Cancer Center, Melbourne, Australia. Immune surveillance and chemo-immunotherapy

Dr Lynton Baird, Malaghan Institute of Medical Research. Carbohydrates in Allergy

April

Dr Arthur Liesz, Translational Stroke Research & Neuroimmunology Research Group, Heidelberg University, Germany. Regulatory T cells are key cerebroprotective immunomodulators in ischemic stroke

Prof Derek Hart, Mater Medical Research Institute, Brisbane, Australia. Antibody to the dendritic cell activation marker CD83 prevents acute graft-versus-host disease and retains T cell immunity

Dr William G Telford, NCI, National Institutes of Health, Bethesda, MD, USA. NZ FLOW CYTOMETRY GROUP MEETING

Dr William G Telford, NCI, National Institutes of Health, Bethesda, MD, USA. Analyzing apoptosis by Flow Cytometry

May

Clare Slaney, Malaghan Institute of Medical Research. The use of immunosuppressive cells to inhibit experimental autoimmune encephalomyelitis

Prof Paul Teesdale-Spittle, School of Biological Sciences, Victoria University of Wellington. Two tifs, too many?

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

Prof Peter Lobie, Associate Director, BCRT Professor of Breast Cancer, Liggins Institute, University of Auckland. Novel therapeutic targets in oncology

Assoc Prof Cristin Print, Molecular Medicine & Pathology, School of Medical Sciences, University of Auckland. Insights into disease through bioinformatics: a critical appraisal

June

Ethan Shevach, National Institutes of Health, Bethesda, MD, USA; Wolfgang Weninger, Centenary Institute, Sydney, Australia; Mariapia Degli-Esposti, Lions Eye Institute, Perth, Australia; Ben Marsland, Nicola Harris, Swiss Federal Institute of Technology, Zurich, Switzerland. NZ ASI BRANCH MEETING

Dr Noriyuki Enomoto, Malaghan Institute of Medical Research. CD8+ T cells ameliorate airway allergic inflammation

July

Dr Richard Cannon, Molecular Microbiology Lab, Dept of Oral Sciences, Dental School, University of Otago. ABC5 and melanoma

Dr Jacquie Harper, Malaghan Institute of Medical Research. Gouty inflammation - bringing clinical, basic and drug development research together

August

Prof Graham Le Gros, Malaghan Institute of Medical Research. Allergens & allergic diseases, what we do know, what we don't know and what we need to find out

Dr Shujie He, Developmental Genetics Lab, Dept of Pathology, Pathology Research Groups, Dunedin School of Medicine, University of Otago. PAX3 and MITF respectively inhibit & promote melanoma cell differentiation

Dr Elizabeth Forbes, Malaghan Institute of Medical Research. Food-induced allergic reactions: Is skin-deep so superficial after all?

Dr Julie Cakebread, Infection, Inflammation & Immunity Division, Southampton General Hospital, UK. The anti-viral and anti-inflammatory effects of inteferon beta (IFN-γ) in asthmatic bronchial epithelial cell cultures

Haley Ataera, Malaghan Institute of Medical Research. The phenotype & function of murine melanoma infiltrating dendritic cells is unaffected by the presence of Foxp3+ Treg

Dr Frank Koentgen, Ozgene, Perth, Australia. Managing mouse GM projects, the science and practicalities

September

Prof Jim McCluskey, Dept of Microbiology & Immunology, Faculty of Dentistry & Health Sciences, University of Melbourne, Australia. Genetic control of T cell immunity: The power of one in combating drugs fat and sugar

Dr Kathryn Stowell, Massey University. Malignant hyperthermia: genetic and biochemical analysis

October

Prof Franca Ronchese, Malaghan Institute of Medical Research. Regulation of the immune response by dendritic cell survival

Dr Bridget Stocker, Malaghan Institute of Medical Research. Small molecules for the treatment of disease

November

Dr Sarah Young, Dept of Microbiology & Immunology, University of Otago. Virus-like particles coupled with proteins are effective immunotherapies against cancer

Dr Melanie McConnell, Malaghan Institute of Medical Research. Cancer stem cells - A research area in need of more controversy

Lisa Connor, Malaghan Institute of Medical Research. Dissecting the protective memory immune response against tuberculosis

Prof John Hamilton, Director, Arthritis & Inflammation Research Centre, University of Melbourne, Australia. Colony stimulating factors, macrophages & inflammatory/autoimmune disease

December

Dr Dan Eilat, Professor of Immunology, Hadassah University Hospital & the Hebrew University Jerusalem, Israel. B-cell tolerance mechanisms in autoimmune New Zealand mice

Prof Zami Ben-Sasson, Immunology & Cancer Research, Faculty of Medicine, Hebrew University of Jerusalem, Israel. The role of IL-1 in CD4 T cell response

2010

January

Dr Mike Berridge, Prof Graham Le Gros, Dr Melanie McConnell, Malaghan Institute of Medical Research. Group Leader's Vision for 2010

February

Prof Franca Ronchese, Dr Jacquie Harper, Dr Joanna Kirman, Malaghan Institute of Medical Research. Group Leader's Vision for 2010

Dr Troels Petersen, Dr Ian Hermans, Dr Bridget Stocker, Malaghan Institute of Medical Research. Group Leader's Vision for 2010

March

Prof Penny Fitzharris, Clinical Director Immunology Department, Auckland Hospital. Food allergy: What's new on the menu?

Joel Zhi-long Ma, Malaghan Institute of Medical Research. The fates of dendritic cells and antigen regulate CD4+ and CD8+ T cell responses

Prof Kurt Kraus, Webster Centre for Infectious Diseases, University of Otago. The Alanine Racemase as a template for antimicrobial drug design

Prof John Miller, Victoria University of Wellington. Mapping the peloruside A binding site on tubulin: Site-directed mutagenesis in yeast

Dr John Fraser, Cytori Therapeutics, San Diego, USA. Adipose tissue as a cell source for regenerative medicine

April

Peter Ferguson, Malaghan Institute of Medical Research. Iron/iron oxide core/shell nanoparticles as contrast agents for Magnetic Resonance Imaging

Dr Jilly Evans, Amira Pharmaceuticals, San Diego, USA. Development of 5-lipoxygenase-activating protein (FLAP) inhibitors for inflammatory diseases

Prof Ian Frazer, Director, University of Queensland, Australia. Day of Immunology public lecture

Prof Ian Frazer, Director, University of Queensland, Australia. Immunotherapy for HPV associated cancer

May

Assoc Prof David Ritchie, Peter MacCallum Cancer Centre, Melbourne, Australia. Immunology adventures in translational haematology

Prof Allan Herbison, Centre for Neuroendocrinology, Dept of Physiology, University of Otago. Kisspeptin Regulation of Fertility: What's all the fuss about?

June

Marina Harvie, Malaghan Institute of Medical Research. Defining the role of CD4 T cells in *N. Brasiliensis* protective immunity

Prof Margaret Brimble, Dept of Chemistry, University of Auckland, Maurice Wilkins Centre for Molecular Biodiscovery. The role of medicinal chemistry in the search for new therapeutic agents: Natural products vs peptides

Dr Ian Hermans, Malaghan Institute of Medical Research. Strategies to enhance CD8+ T cell responses to vaccination

July

Ed Pearce & Erika Pearce, Trudeau Institute, New York, USA; Alan Baxter , James Cook University, Queensland, Australia; Carola de Vineusa, The John Curtin School of Medical Research, Canberra, Australia. NZ ASI MEETING

Dr Bob Anderson, Lab Head Autoimmunity and Transplantation Division, WEHI, Melbourne, Australia. Translating discovery of "toxic gluten peptides" to a peptide immunotherapy for coeliac disease

Dr Joanna Kirman, Malaghan Institute of Medical Research. Memories are made of this: memory CD4+ T cell subsets that protect against mycobacterial infection

FUNDRAISING & COMMUNICATIONS REPORT

As Fundraising & Communications Manager, I have seen tremendous growth of the department during 2009 and 2010 with our staff numbers essentially doubling. Firstly, in January 2009 we welcomed Vicky Hale to the Wellington Office as Marketing Administration Assistant and later in the year an Auckland based team member, Annabel Lush, who has taken up the challenge of raising our profile in the Northern Region. Staff numbers then took a temporary decrease with my departure on maternity leave in early 2010 – though I left the reins in very capable hands during my absence. Not only were all the regular projects successfully completed, but several new initiatives were also implemented such as the Alumni communications e-magazine 'Malaghanite' and the monthly e-update 'Focus'. I would like to thank my hard-working team for their contributions to a fantastic past nineteen months for the Fundraising & Communications department.

Also deserving of our sincerest thanks are the dedicated Friends committees around the country – including our newest addition in Taupo. These hard-working individuals give their time tirelessly each year in organising the many fundraising events held on behalf of the Institute. In fact, the past nineteen months have been the busiest for these Friends committees for quite a few years, so thank you all very much!

Some interesting facts about this reporting period:

- Approx $84,000 was raised collectively from the two Lollipop Street Appeals in Feb 2009 and Feb 2010
- In order to achieve this, we had over 250 wonderful volunteers manning the streets with buckets and lollipops throughout the Greater Wellington region for each appeal
- 25 tour groups visited our facilities and 30 community groups were visited by one of our scientists
- Over 100 visitors came through the doors on our Open Day in August 2009
- Over $190,000 was received in donations via our four mail appeals during 2009, with another $100,000 received by 31 July 2010
- To reach this outstanding total, approx 4200 individual donations were generously given
- Collectively, the Charity Golf Tournaments organised by the Friends Committees raised over $100,000
- In addition to the golf tournaments, the four regional Friends committees held or assisted with another six events to raise funds for, or awareness of, the Institute's research programmes

We can see from this that the Malaghan Institute is extremely fortunate to have such loyal volunteers, supporters and donors who support our work.

All of the funds raised go directly towards supporting our 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 work would stop, so thank you very much to all of you who have shown your commitment to our organisation this year.

Tanya Fulcher, Vicky Hale, Annabel Lush,
Dr Debbie Scarlett, Jacqui Whelan

FUNDRAISING & COMMUNICATIONS

FRIENDS OF THE MALAGHAN INSTITUTE

Wellington Friends

Robyn Vavasour (Chair) (to May 2010)

Judy Blair

Adrienne Bushell

Maureen Cameron

Gaye Carroll

Sylvia Goldman (to Nov 2010)

Jill Kinloch

Susan Laurenson (Chair) (from Jun 2010)

Emma Lawler

Carol Martin

Merrilyn O'Sullivan

Suzanne Szusterman

Denise Udy

Wellington Functions 2009/10

Lollipop Street Appeal 2009

Port Nicholson Rotary Charity Dinner & Auction

ING NZ Ltd Malaghan Golf Tournament

Lollipop Street Appeal 2010

Rotary Club of Wellington Jumbo Tennis 2010

Fashion for Research Fashion Show

Hawkes Bay Friends

David Mossman (President)

Denise Bull (Chair)

Margie Dick

Beth Kay

Bry Mossman

Andy Neilson

Rosemary O'Connor

Jan Paterson

Bruce Speedy

Lynn Spence

John Stovell

Terry Thornton

Caroline Walton-Green

Hawkes Bay Functions 2009/10

Malaghan Institute Golf Tournament

Auckland Friends

Beverley Ferguson

Trudi Gardner

Tania Glanfield

Elaine Haggitt

Margaret Malaghan

Jane Parlane

Raewyn Roberts

Auckland Functions 2009/10

AMI Insurance Malaghan Golf Tournament

Engines Running Hot Fashion Event

Taupo Friends

Anne Velvin (Chair)

Rick Hart

Merryn Herrick

Caroline Martin

Kathryn Uvhagen

Adele Wilson

Doug Wilson

Taupo Functions 2009/10

Tui Golf Tournament – nominated charity

Taupo Friends 'Meet the Director' Cocktails

FUNDING SOURCES

Thank you to the following individuals, organisations, businesses, Trusts and Foundations who helped support the Malaghan Institute from 1 Jan 2009 – 31 Jul 2010:

Grants, Trusts and Foundations

Arthur N Button Charitable Trust
Carol Tse (No.2) Family Trust
Clyde Graham Charitable Trust
Cuesports Foundation Ltd
Dorothy Eden Trust
Gadbrook Trust
Infinity Foundation Ltd
John Holt Memorial Trust
KIA Taylor Trust
Lion Foundation
Margaret Neave Charitable Trust
Nikau Foundation
PO Bennett Trust
SE Leuchars Family Trust
Springhill Charitable Trust & Frimley Foundation
The Great New Zealand Trek Charitable Trust Inc.
The Keith Seagar Research Fund
The Nick Lingard Foundation
The Paddy Brow Charitable Trust
The Southern Trust
Woodlands Trust

Major Corporate Sponsors

AMI Insurance Ltd
Clemenger BBDO
Frank Millar & Co (Wgtn)
Just Paterson Real Estate
NOW Couriers
Spy Valley Wines

Corporate Donors

Blair Gowrie Investments
BNP Paribas Security Services
Brooklands Land Company Ltd
Buzz Channel Ltd
Macquarie Group Foundation
Monteiths Brewery Bar Khandallah
Nichecom
Pacific Radiology Limited
The Art of Giving Limited
Tophouse Team
Wairakei Tui Golf Club
Whakatu Coldstores Limited

Event Supporters & Sponsors

Alan Chapman
All About Beauty
Alligator Security
Ambeli Restaurant
AMI Insurance Ltd
AMP Capital Investors
AMPS (Auckland Motorcycles & Power Sports)
Andy Gall Designer
Annie Hodgkinson
Antipodes NZ Ltd
ANZ Banking Group
Barfoot & Thompson
Bay Ford Hastings
Bay Plaza Hotel
Bayleys CD Realty (HB) Ltd
BDO Spicers
Beaute of Kelburn
Beleza
Bennetts
Big Picture Wine
Blackmores
Blue Cactus Hairdressing
Blue Moon
Bobbi Gibbons
Body Magic
Boulcott Street Bistro
BP Oil NZ
Brittain Wynyard
Bryan & Jan Johnson
Business Management Services Ltd
Cable Bay Vineyard
Cadbury Confectionery Ltd
Caffe L'Affare
Cameron Brewer
Cameron Partners
Cape Kidnappers
Capital Construction
Cerise Clothing
Chicago Menswear
Chop Hairdressing
Chrissie Moore Interiors
Circa Theatre
Coca-Cola Amatil Ltd
Colin Blair & Team
Connells Bay Sculpture
Constellation Wines
Cottages New Zealand Ltd
Craggy Range Winery
Datamail
Datastor
David Taylor & Team
David's Hairstylists Ltd
Delmaine Fine Foods
Deus Ex Machina
Di & John Conway
Diva Restaurant & Lounge
Downstage Theatre
Driftwood Lodge
Drillers Poultry Farm
Eagles Nest Resort
Elizabeth Horne
Esteem Jewellery
Eurowines Fine Wines
Farmlands Trading Society Ltd
Fern Ridge Ltd
Fonterra Brands (TipTop) Ltd
Forbes and Co.
Freyberg Gym
Glengarry – Thorndon Quay
Goldman & Associates Ltd
Gordons Outdoor Equipment
Grande Gourmet Ltd
Greenfernz
Grouse Lighting
Hastings Pro Shop
Hawkes Bay Insurances
Hawthorne Coffee Roasters Ltd
Health 2000
Hemisphere Freight
Hill Seekers
Hodgies Fresh Fruit
Hotel Intercontinental
HSBC
Ian Lindsay & Team
Industrial Processors Ltd
ING NZ Ltd
Inspire Photography
James Coleman
Jane & Paul Wright
Jeff Gray European Ltd
JJ Catering
John & Glen Towns
John Holt Memorial Trust
Just Paterson Real Estate
Kapiti Oil
Karori Flower Shop
Kay Geor
Kemblefield Winery
Kevin O'Connor & Team
Khandallah Pharmacy
Kiely Thomson Caisley
Kinloch Golf Course
Kohi School
Krystal Foss
Lexus of Wellington
Little India, Wellington
Lowe Corporation Ltd
Loyalty NZ Limited
Lynn & Alistair Spence
Magz2u Magazines
Manor Park Golf Club
Maria Pia's Trattoria
Mark Howard
Martha's Pantry
Martin Bosely's Yacht Club Restaurant
Matangi Farm Cottage
Matariki Wines Ltd
Mazda Motors NZ Ltd
Mercury Bay Golf Club
Mi Piaci
Michael's Catering
Millar Road
Museum Hotel
National Livestock
Nelson & Simich Ltd
Nestlé New Zealand Limited
Nice & Natural
NOW Couriers
NZ Symphony Orchestra
Olive Tree Cafe
OMD Wellington
OM Financial
Onesource Ltd

Opus International Consultants
Oracle New Zealand
Orb Communications
Orton Catering Ltd
Pak n Save, Hastings
Pak-Line
Parker and Associates
Pearson Investment Advisory
Penny Kember Design
Petrena Miller Design
Plan B
Plum Cafe
Port Nicholson Rotary Club
Port of Napier
Porter Hire
Quest Hotels
Rainbow Print
Regal Haulage
Richard Laurenson
Rosemary O'Connor
Rotary Club of Wellington
Rupert Ryan
Salon Gowrie
Samson & Delilah
Scent Floral Boutique
Scholastic New Zealand
Senate Communications
Shott Beverages
Signwise Auckland
Sileni Estates Winery
Silverdale Knitwear
Smith & Smith Ltd
Spiegelau NZ
St Martin Vineyard House
Stevenson Group Limited
Strawberry Fare
Telegraph Hill Olives
The Australian High Commission
The Beach Hut
The Block Shop
The Cut Magazine
The Designer Clothing Gallery
The Diamond Shop
The Grange Golf Club
The Lost Springs Spa
The Mews
The Terrace Conference Centre
Thompson Suits
Toms Cottage
Tracey Russell
Tuahu Farmstay
Tui Oaks Hotel
Tunanui Farmstay Cottage
Turners and Growers
Two Souls Bistro
Urban Retreat, Hastings
Urban Sanctuary Beauty Clinic
Vance Vivian
VetEnt Napier
Veterinary Associates Hastings Ltd
Vista Restaurant
Wairunga Golf Course
Wakefield Health Ltd/Royston Hospital
Wellington Bridge Club
Wendy & John Thompson Trust
West Plaza Hotel
White House Restaurant
Working Style

Special Donors

J Arbuckle
Kylie Archer – ran NY Marathon
Richard Barr – walked UK
A Bidwill
E Bidwill
J Butcher
A Chapman
A & J Cockburn
J Crosse
P Darney
M Farrelly
B Flynn
J & J Frizzell
B Gestro
N Gillies
R Gordon
R Greenwood
A Harpur
Kate Haselhoff – shaved her head to fundraise for cancer research
J Holdsworth
S Iorns
F Lee
W Leslie
Lions Club of Kapiti Pakeke
Lodge Homewood No 447
M Malaghan
H McKendrey
R Mansfield
P Mead
H Michel-Fleurie
O Nees
R Pilgrim
D Plunkett
B & A Pocock
H & B Romanes
Rotary Club of Port Nicholson
N Smith
St Lukes Mission Guild
R Stannard
The Johnson Charitable Trust
C Thompson
I Thompson
C Tisdall
Titahi Bay Wellness Group
N Todd
J Todd
W Tucker
Waikanae Auxiliary Cancer Society
A Walbridge
J Wallace
M Wallace
V Ward
M Wilkes
M Wilkinson
C Williams
Dave Wilson – walked England

Bequests

The following people left bequests to the Institute:

BEA Trust
BEARD 42 Charitable Trust
Ann Callaghan-Millage
WA Clark
Graham John Hall
Isabella McKenzie Morgan Charitable Trust
Arnold Peter Jagger
Dennis Lamb
Ruth Elna Penberthy
Mary Rei Preston-Thomas
Hugh Rolleston Prickett
Ernest Reid Robinson
Mervyn Shaw
Robert Clyde Smith
Marjorie Janice Staffan
BB Stoker
Graeme William Thomson
Hilary Ann Willberg
Eileen Elsie Worrall

In Memoriam Donations

Donations were received in memory of the following people:

Kit Barrington
Graeme L Birdsall
Bill Blair
Sandy Campbell
Stella Daniell
Marjorie E Dellabarca
Ngaire J Dentice
Mariott Eady
Michael Forrestal
Jack Gardner
Graeme Geary
Michele Gestro
John Harrison
Phyllis B Hastings
Bessie J Honore
Lucy Ingpen
John Logan
Andrew Lynch
Marilyn Mather
Keith Nicholls
Jack O'Neill
Keith Parker
Sally R Paterson
Hugh Prickett
Tom Reid
Ivy Joan Robertson
Ross Ronowicz
Brian Tolley
Joyce N Waddell
Ian Ward
Betty Ward
Daniel G Whibley
Anne Williams

RESEARCH GRANTS

AgResearch Ltd Hamilton
To Prof Le Gros to support the project "Immunomodulation of the inflammatory responses that result from adverse reactions to milk"

Arthritis New Zealand
To Dr Harper to support the project "Impact of hyperuricaemia on monocyte/macrophage phenotype in gouty arthritis"

Breast Cancer Research Trust
To Prof Berridge and Dr McConnell to support the project "Unleashing the power of the immune system on breast cancer"

Cancer Society of New Zealand (National Body)
To Prof Ronchese and Dr Kirman to support the project "Using the power of Mycobacteria to boost anti-tumour immunity"

To Prof Berridge and Dr Hermans to support the project "Targeting tumour stem cells to improve immunotherapy"

To Prof Berridge and Dr Stocker to support the project "The synthesis of Ascidiathiazone B and analogues thereof, for PMET drug-based cancer therapy"

To Dr Stocker and Dr Hermans to support the projects "Glycolipid adjuvants: enhancing cancer vaccines" and "Mechanisms of induction of anti-tumour responses by dendritic cells"

To Dr Hermans to support the project "Using dendritic cell immunisation to sensitise malignant glioma to chemotherapy"

Cancer Society of New Zealand (Wellington Division)
To Prof Ronchese to investigate the "Accumulation of regulatory T cells in tumour bearing mice"

Child Health Research Foundation
To Prof Le Gros and Prof Berridge to support the project "Activating the immune system against cancer: Application of dendritic cell immunotherapy to childhood brain cancers & central nervous system leukaemia"

Fonterra Co-operative Group Ltd
To Prof Le Gros to support the project "Anti-allergy effects of dairy ingredients"

Foundation for Research Science & Technology
To Prof Le Gros to support the project "Assessing the activation of Tregs by cow and goat -lactoglobulin in the optimized IPIG model using GFP-reporter mice"

To Dr McConnell, Dr Harper and Dr Herst to support an investigation into the "Immunomodulatory effects of NZ native honey, using *in vitro* studies & mouse models of acute inflammation"

To Dr Kirman to support the project "Characterising protective CD4+ memory T cell subsets that mediate protection against Tuberculosis"

To Dr Hermans and Dr Harper to support the project "Carbohydrate nanotechnology - large, carbohydrate containing immuno-pharmaceuticals"

To Dr Harper to support the project "Berry fruits for treating inflammation"

Genesis Oncology Trust
To Prof Berridge to support the project "Metabolic constraints on tumour metastasis"

To Prof Ronchese and Dr Weinkove to support the project "Phenotype and function of invariant natural killer T cells in chronic lymphocytic leukaemia"

Haematology Society of Australia & New Zealand
To Prof Ronchese and Dr Weinkove to support the project "Effect of invariant natural killer T cell stimulation on dendritic cell function in chronic lymphocytic leukaemia"

Harry & Beverley Romanes
To Prof Le Gros to support the project "The effect of the novel immune suppressive agent FTY720 on allergic airway disease"

Health Research Council of New Zealand
To Prof Le Gros and Dr Forbes to support the project "New strategies for treatment and prevention of food allergy"

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

To Prof Ronchese and Prof Le Gros to support the project "Role of dendritic cells in allergic sensitisation"

To Prof Ronchese to support the project "Defining the characteristics of effective anti-tumour T cells"

To Dr Hermans, Dr Petersen and Dr Stocker to support the project "Mechanisms of induction of anti-tumour immune responses by dendritic cells"

To Dr Hermans to support the projects "Novel magnetic nanoparticles as contrast agents for magnetic resonance imaging" and "Improving immunotherapy for high grade glioma"

To Dr Harper and Dr Martin to support the project "Nga wai o Rongo"

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

Industrial Research Ltd/Viclink Ltd/Grow Wellington
To Dr Hermans, Dr Harper and Dr Stocker to support the project "DC vaccine adjuvant"

Keith Seagar Research Fund
To Prof Le Gros and Prof Ronchese to support cancer research

KIA Taylor Trust
To support the development of the Keith & Faith Taylor Cancer Research Laboratories

Leukaemia & Blood Foundation of New Zealand
To Prof Ronchese and Dr Weinkove to support the project "Harnessing invariant natural killer T cells to treat chronic lymphocytic leukaemia"

Marjorie Barclay Trust
To Prof Le Gros to support asthma research

Maurice Wilkins Centre
To Prof Ronchese and Dr Hermans to support the project "Immune responses in mouse lymph nodes"

To Prof Le Gros and Dr Kirman to support the project "Development & testing of novel DNA and protein 'dormancy' vaccines against *Mycobacterium tuberculosis*"

Melanoma Research Alliance
To Prof Berridge, Dr McConnell and Dr Petersen to support the project "Therapeutic targeting of melanoma stem cells"

Motor Neurone Disease Association of New Zealand - The estates of Ellen, Sinclair, Barbara and Alison Wallace
To Dr McConnell to support the project "Sirt 1 Protein"

New Zealand LAM Trust/LAM Australasia Research Alliance
To Prof Berridge to support the project "Self-renewal properties of LAM cells"

New Zealand Lottery Health Research
To Prof Le Gros and Dr Stocker to support the project "A sweet solution to asthma"

To Prof Le Gros and Dr Forbes-Blom to support the project "Getting to the guts of allergic inflammation"

To Prof Ronchese to support the project "Interactions between regulatory T cells and dendritic cell cancer vaccines"

To Dr Stocker and Dr Kirman to support the project "Alkenylamine inhibitors of *M. tuberculosis"*

To Dr Harper to support the project "Nk1.1 upregulation on MSU-activated macrophages"

To Dr Kirman to support the projects "Advancing vaccination against Tb: Why helminth infection impairs BCG's efficacy" and "Identifying memory CD4+ T cell subsets that protect against Tuberculosis"

To Dr McConnell to support the project "Are SOX2-positive tumour stem cells responsible for tumour formation?"

To Dr Hermans and Dr Stocker to support the project "Stimulating immune responses to tumours with modified ganglioside-based glycolipids"

To Dr Harper (originally to Assoc Prof Bäckström) to support the project "The role of regulatory T cells in multiple sclerosis"

Neurological Foundation of New Zealand
To Dr Hermans and Mr Hunn to support the project "Dendritic cell therapy for glioblastoma multiforme"

Rex and Betty Coker Scholarship
To Prof Le Gros to support PhD scholarships

Robert McClelland Trust
To Dr Hermans and Mr Hunn to support the project "Dendritic cell therapy for glioblastoma multiforme

Roy McKenzie Medical Research Fellowship
To Dr McConnell to support the project "Exploiting deacetylase activity to enhance anti-cancer drug efficacy"

Royal Australasian College of Surgeons
To Mr Hunn to support the project "Dendritic cell therapy for high grade glioma"

Surgical Research Trust
To Mr Hunn to support the project "Dendritic cell therapy for high grade glioma"

The estates of Ellen, Sinclair, Barbara and Alison Wallace
To Dr McConnell to support the "Stem cell research" programme

The Graham Hall Bequest
To Mr Hunn to support the project "Dendritic cell therapy for high grade glioma"

The Great New Zealand Trek Charitable Trust Inc
To support MS research being undertaken by Dr Anne La Flamme

The Royal Society of New Zealand Marsden Fund
To Prof Le Gros and Prof Ronchese to support the project "Th1 or Th2 responses: a matter of dendritic cell life or death"

To Prof Berridge to support the project "Interfaced nanobiosystems: communicating with cells using embedded nanostructures"

To Dr Petersen, Dr Hermans and Dr Kirman to support the project "Towards better vaccines: Investigating the role of langerin+ CD8+ dendritic cells in innate and adaptative immunity"

Wade Thompson
To support the Cancr Vaccine Programme

Wellington Medical Research Foundation
To Prof Ronchese to support the projects "Mechanisms of dendritic cell killing by effector CD8+ T lymphocytes" and "Characterisation of dendritic cells cultured in Flt3L for tumour immunotherapy"

To Prof Berridge to support the projects "Investigating immunotherapy targeted at tumour stem cells within brain tumours" and "Self-renewal properties of LAM cells"

To Dr Hermans to support the project "Exploiting different mechanisms of inducing anti-tumour immune responses by dendritic cells"

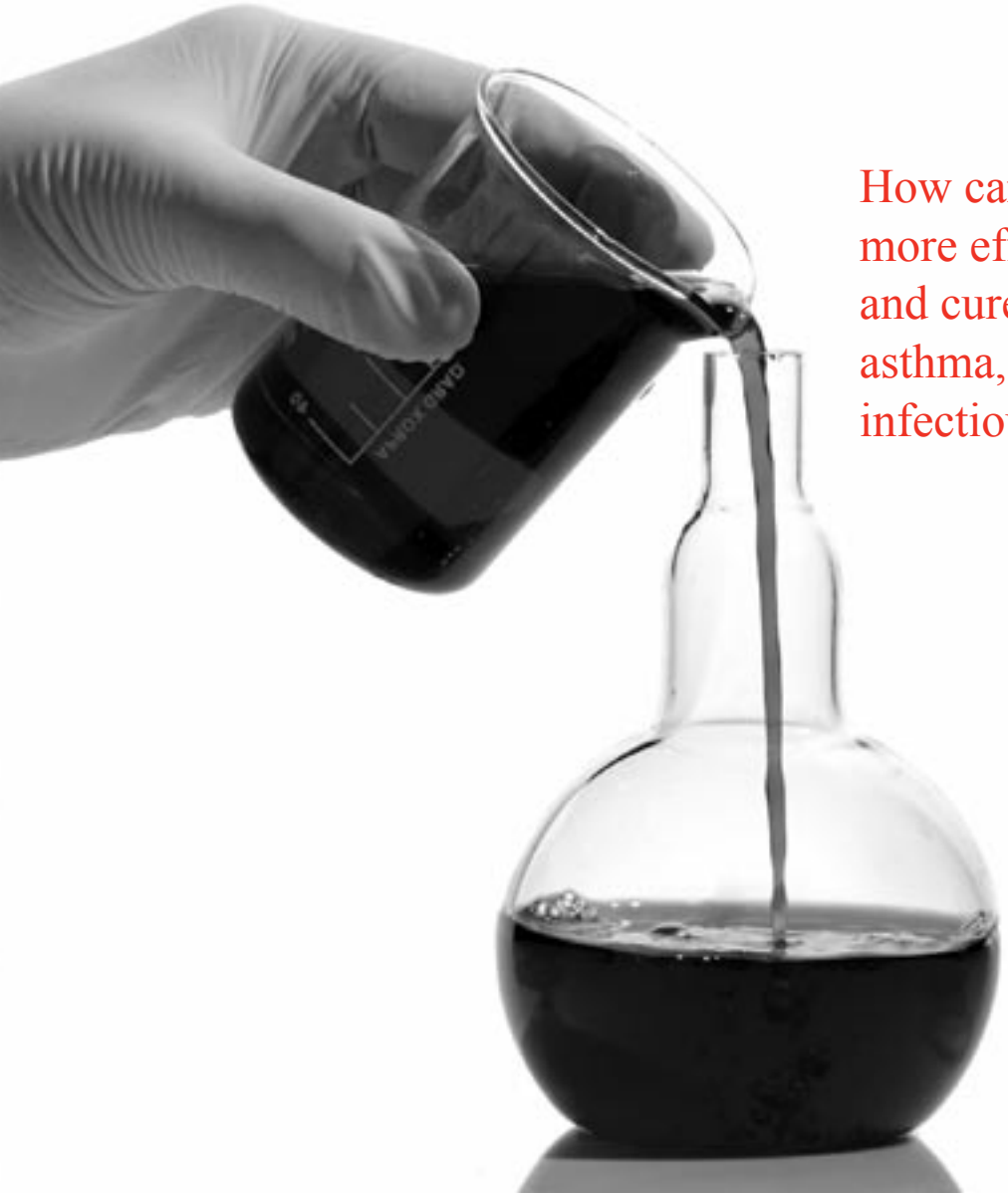
To Dr Hermans and Dr Petersen to support the project "Characterisation of cross-presenting langerin-positive dendritic cells in the spleen"

To Dr Harper to support the project "Role of the kinin-kallikrein system in an animal model of acute gouty arthritis"

To Dr Kirman to support the project "Characterising protective CD4+ memory T cell subsets that mediate protection against Tuberculosis"

To Dr Stocker to support the project "Imino sugars as inhibitors of *M. tuberculosis* - biological evaluation of a new class of Mycobacterial arabinan biosynthesis inhibitors"

HOW CAN YOU HELP?



How can you help us find more effective treatments and cures for 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 goal 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 the research programmes 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.

Donations

Donations from individuals and Trusts form a vital 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 dependent on bequests. We have developed an endowment fund that will grow from major gifts and bequests, hence sustaining the future of the Institute.

To assist you in leaving a gift to the Malaghan Institute, we offer the following format:

"I bequeath to the Malaghan Institute of Medical Research

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

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"

The information above is a guide only and is not intended as specific legal advice. Please consult your own legal advisor.

Should you require any additional information about the above options 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 6914

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

FINANCIAL REPORT

The past twelve months has seen our grant income increase as our Institute continues to expand

This growth in grant funding has seen the salaries and research expenses also increase. In order to fund the necessary infrastructure to support our growth we look to the Capital Endowment Fund in various ways to "plug the gaps" in our funding. As previously, it has continued to provide day to day funding by passing through to the Institute the income it has earned on investments. This year, in addition to this, it has provided $245k for the funding of our new laboratories.

The Capital Endowment Fund has held its value in these recessionary times. The fund is currently at just over $5m thanks to the prudent management provided by our advisors and our Investment Committee.

The funding of fixed assets is always a challenge. This year has been no exception. The Institute has received funds for major fixed asset purchases of $448k and a further $68k for smaller equipment items. This left a shortfall of $84k that the Institute has funded.

Last, but not least, our donors have contributed almost $600k to fund science. Supporters of the Institute have, through their wills, provided $265k of bequests during the past 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 Malaghan Institute of Medical Research (the "Institute") and Group for the year ended 31 July 2010.

This report is provided solely for your exclusive use and solely for the purpose of providing an opinion on the summary financial statements. Our report is not to be used for any other purpose, recited or referred to in any document, copied or made available (in whole or in part) to any other person without our prior written express consent. We accept or assume no duty, responsibility or liability to any other party in connection with the report or this engagement, including without limitation, liability for negligence.

Trustees' Responsibilities

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

Auditor's Responsibilities

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

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 financial statements are 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 the Institute 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, the Institute and Group's full audited financial statements contain 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 and upon which we expressed a qualified audit opinion in our report to the Trustees dated 1 October 2010.

For a better understanding of the scope of our audit of the Institute and Group's financial statements and of their financial position, financial performance and cash flows for the year ended 31 July 2010, this report should be read in conjunction with the Institute and Group's audited financial statements for that period.

Our examination of the summary financial statements was completed on 1 October 2010 and our qualified opinion is expressed as at that date.

Chartered Accountants
WELLINGTON, NEW ZEALAND

FINANCIAL REPORT

Malaghan Institute of Medical Research
- Summary Financial Statements 2010

Consolidated Summary Statement of Financial Performance For the year ended 31 July	**2010 Consolidated** 12 months to 31/7/10	**2009 Consolidated** 7 months to 31/7/10
Income - Operating		
Income from Donations	596,378	259,917
Income from Scientific Grants	5,061,196	2,901,411
Sundry Income and Interest from Investments	301,149	64,650
	5,958,723	3,225,978
Expenses - Operating		
Salaries	3,442,241	1,827,245
Depreciation	587,904	396,103
Other expenses	3,114,920	1,728,631
	7,145,065	3,951,979
Operating (Deficit)	**(1,186,342)**	**(726,001)**
Grant Income for Fixed Asset Purchases	448,415	31,765
Net (Deficit)/Surplus	(737,927)	(694,236)
Capital Endowment Fund		
Investment Income	311,718	212,440
Bequests	265,273	176,060
Net Income	576,991	388,500

Consolidated Summary Statement of Movements in Equity For the year ended 31 July	2010 Consolidated 12 months to 31/7/10	2009 Consolidated 7 months to 31/7/10
Opening Balance	6,071,784	6,377,520
Net (deficit)/surplus for the year		
- Operating Income	(737,927)	(694,236)
- Capital Endowment Fund	576,991	388,500
Total recognised income and expenditures	(160,936)	(305,736)
Total Funds	5,910,848	6,071,784

Consolidated Summary Statement of Cash Flows For the year ended 31 July	2010 Consolidated 12 months to 31/7/10	2009 Consolidated 7 months to 31/7/10
Net Cash Flow from Operating Activities	456,794	233,101
Net Cash Flow from Investing Activities	(614,510)	(372,532)
Net Increase in Cash Held	(157,716)	(139,431)
Cash at Beginning of the Year	2,288,277	2,427,708
Cash at End of the Year	2,130,561	2,288,277
(Funds committed to scientific research by grantors)		

Consolidated Summary Statement of Financial Position As at 31 July	31 July 2010 Consolidated	31 July 2009 Consolidated
Current Assets	4,212,308	4,973,200
Current Liabilities	(3,219,422)	(3,358,148)
Fixed Assets	1,617,844	1,606,606
Investments	3,300,118	2,850,126
Total Equity	5,910,848	6,071,784

Presented above are the Summary Financial Statements of the Malaghan Institute of Medical Research (the "Institute"), a not for profit entity, for the year ending 31 July 2010 which were extracted from the full Financial Statements authorised for issue by the Trust Board on 1 October 2010. A qualified audit report was issued on 1 October 2010.

The Institute qualifies for differential reporting by virtue of the fact that it is not publicly accountable and does not qualify as large. All differential reporting exemptions available have been applied in the preparation of these financial statements with the exception of FRS- 10: Statement of Cash Flows.

The full Financial Statements have been prepared in accordance with NZ GAAP. 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"), rounded to the nearest dollar.

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

DIRECTORY

Board of Trustees

Mr Graham Malaghan *FCILT, PhD(VUW) honaris causa (Chairman)*

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Mr Gary Quirke *BCA, CA, FCILT*

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Mr C Dan Williams *CA*

Staff of the Institute 2009/10

SCIENTIFIC

Director of Research

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

Group Leaders

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

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

Dr Ian Hermans *BSc(Hons)(Otago), MSc(Distinc)(Otago), PhD(VUW)*

Dr Joanna Kirman *BSc(Hons), PhD(Otago) - WMRF Malaghan Haematology Fellow*

Dr Melanie McConnell *BSc(Hons), PhD(Otago) (from Jul 2010)*

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)*

Senior Research Fellows

Dr Melanie McConnell *BSc(Hons), PhD(Otago) (to Jun 2010)*

Dr Troels Petersen *MSc, PhD(Copenhagen) - Regulatory Affairs Officer (from Jul 2010)*

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

Research Fellows/Post-doctoral Research Fellows

Dr Lynton Baird *BSc(Hons)(Otago), PhD(VUW) (to Dec 2009)*

Dr James Baty *BSc(Hons)(VUW), PhD(Otago) (from Feb 2009)*

Dr Noriyuki Enomoto *MD, PhD(Hamamatsu, Japan) (to Oct 2009)*

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

Dr Marina Harvie *BSc(Hons), PhD(VUW) (from Jun 2010)*

Dr William John Martin *BSc, MSc(Hons)(Waikato), PhD(VUW) (from Mar 2009)*

Dr Heli Matilainen *MSc, PhD (Jyvaskyla, Finland) (from Jul 2009)*

Dr Ben Mulchin *BScTec(Hons)(VUW), PhD(Massey) (to Oct 2009)*

Dr Troels Petersen *MSc, PhD(Copenhagen) - Regulatory Affairs Officer (to Jun 2010)*

An Tan *BSc(VUW)*

Visiting Researchers

Dr Scott Harding *MBChB(Otago), FRACP (P/T) (to Jan 2009)*

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

Dr Anil Ranchord *MBChB(Otago) (to Jan 2009)*

Clinical Research Fellows

Dr Peter Ferguson *MBChB(Otago)*

Dr Rebecca Grainger *BMedSci(Distinc), MBChB(Distinc) (Otago), FRACP (to Jul 2009)*

Mr Martin Hunn *MBChB(Otago) FRACS (from Feb 2009)*

Dr Robert Weinkove *MA(Cantab), MBBS(London), MRCP(UK), FRCPath(UK)*

Staff Scientists

Evelyn Bauer *NZCSc, Cert Animal Sci & Tech(Massey) - GMP Production Manager*

Nicola Kofoed *BSc, DipGrad(Otago) - Manager BRU (to May 2010)*

Hannah Larsen *BSc(Queensland) (from May 2009) - BRU Deputy Manager (from May 2010)*

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

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

Senior Research Officers

Kate Broadley *BSc(Massey) (from Jul 2010)*

Mali Camberis *BSc(VUW) (P/T)*

Kathryn Farrand *MSc(Massey)*

Evelyn Hyde *MSc(Distinc)(Otago)*

Deborah Knight *MSc(Otago) (from Jul 2010)*

Melanie Prout *BSc(Hons)(VUW) (P/T)*

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

Odette Shaw *BSc(Hons)(Otago) (from Jul 2010)*

Dr Jianping Yang *MB(Shanxi Medical University)*

Research Officers

Kate Broadley *BSc(Massey)(to Jun 2010)*

Clarissa Chandrahasen *BBmedSc(VUW) (to Dec 2009)*

Janice Cheng *BBmedSc(Hons)(VUW) (Jan-Dec 2009)*

Hilary Corkran *BSc(Hons)(Massey) (from Mar 2010)*

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

Hannah Kelly *BBmedSc(Hons)(VUW) (from Feb 2009)*

Deborah Knight *MSc(Otago) (to Jun 2010)*

Brigitta Mester *MSc(Hungary)*

Gert-Jan Moggré *BSc (Netherlands) (from Jun 2010)*

Catherine Plunkett *BBmedSc(Hons)(VUW) (from Feb 2010)*

Lisa Shaw *BSc, MSc(Otago) (from Feb 2010)*

Odette Shaw *BSc(Hons)(Otago) (Aug 2009 - Jun 2010)*

Ching-Wen Tang *MSc(Otago) (from Jan 2010)*

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

Dr Mischa Walton *MSc(Friedrich-Schiller, Germany) PhD(Massey) (P/T) (to Mar 10)*

Research Assistants

Sharon Brokenshire *(to Dec 2009)*

Stephanie Chee *(from Mar 2010) (P/T)*

Charlotte Cheriton - *Administration Manager BRU*

Amy Doyle *BSc(VUW) (to Jan 2010)*

Ben Harvie *NZ Dip Bus(Whitireia) (from Feb 2010)*

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

Kelly Locke

Katherine MacGregor *BSc(Massey) (to Apr 2009)*

Laura McVeigh *BSc(Hons)(Leeds University, UK) (from Dec 2009)*

Amanda Payne *BSc(Otago)*

Ashlie Price *BSc(VUW) (from Mar 2010)*

Research Nurse

Catherine Wood *RN, BN, PGDipHealSci*

PhD Students

Lindsay Ancelet *BSc(Hons)(USask, Canada), MSc (Toronto,Canada) (from May 2009)*

Haley Ataera *BSc, MSc(VUW) (to May 2010)*

Janice Cheng *BBmedSc(Hons)(VUW) (from Jan 2010)*

Lisa Connor *BBmedSc(Hons)(VUW) (to Nov 2009)*

Emma Dangerfield *BBmedSc(Hons)(VUW)*

Nina Dickgreber *DipSci(Kiel) (to Jul 2009)*

John Gibbins *BBmedSc(Hons)(VUW) (from Feb 2010)*

Marina Harvie *BSc(Hons)(VUW) (to Jun 2010)*

Gregory Haslett *BSc(Hons)(VUW) (from Jan 2010)*

Ashna Khan *BSc(USP, Fiji),PGDip(Auckland), MSc(VUW)*

Sabine Kuhn *Diplom Biologie(LMU Munich, Germany) (from Mar 2009)*

Sara McKee *BSc(Hons)(Otago) (from Jun 2010)*

Rene McLaughlin *BBmedSc(Hons)(VUW) (from Jan 2010)*

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

William John Martin *BSc, MSc(Hons)(Waikato) (to Mar 2009)*

Helen Mearns *BSc(Hons), MSc (University of Cape Town, RSA)*

Taryn Osmond *BBmedSc(Hons)(VUW) (from Feb 2010)*

Marie Petrie-Deely *BBmedSc(Hons)(VUW) (from Nov 2009)*

Kelly Prendergast *BBmedSc(Hons)(VUW) (from Jan 2010)*

Marcus Robinson *BBmedSc, MSc(Hons)(VUW) (from May 2009)*

Janelle Sauvageau *BSc, MSc (UL, Canada) (from Oct 2009)*

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

Helen Simkins *BSc(Hons)(Otago) (to Jan 2010)*

Clare Slaney *BSc, MSc(Hons)(Auckland) (to Feb 2010)*

Stefanie Steiger *DipSci(MLU, Germany) (from Sep 2009)*

Anna Win-Mason *(BSc)(Hons)(VUW)*

Masters Students

Susanna Brow *BSc, BBmedSc(VUW) (from Jan 2009)*

Sonai Lim *BBmedSc(VUW) (from May 2009)*

Tommy Liu *BSc(Otago), Grad dip BBmedSc(VUW) (to Dec 2009)*

Aras Toker *BSc(Germany) (to Apr 2009)*

Honours Students

Rachel Hunter *(to Dec 2009)*

Aidan Leong *BSc(VUW) (Mar - Nov 2009)*

Taryn Osmond *BBmedSc(VUW) (Mar - Nov 2009)*

Catherine Plunkett *BBmedSc(VUW) (Mar – Nov 2009)*

Visiting Students

Gert-Jan Moggré *(Aug 2009-Jun 2010)*

Stefan Munneke *BSc(Netherlands) (from Jul 2010)*

Stefanie Steiger *DipSci(MLU, Germany) (to Jan 2009)*

Summer Students 2009/2010

Alanna Cameron

Stephanie Chee

Jack Du

Sonai Lim *BBmedSc(VUW)*

Samuel Nobs

Bryan Northover *BSc(VUW)*

Taryn Osmond *BBmedSc(Hons)(VUW)*

Catherine Plunkett *BBmedSc(Hons)(VUW)*

SCIENCE SUPPORT AND ADMINISTRATION

Administration

Carolyn Hallsmith - *Receptionist (P/T)*

Federico Iglesias *BCA(Hons)(UADE, Argentina) - Administrative Assistant (from Apr 2010) (P/T)*

Finance

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

Susie Whelan *CA, NZIMDip - Finance Manager*

Fundraising & Communications

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

Victoria Hale *BCA, BSc(VUW) - Marketing Administration Assistant (from Jan 2009)*

Annabel Lush *LLB, Dip Bus (Marketing)(Auckland) - Northern Region Development Coordinator (from Aug 2009) (P/T)*

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*

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

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

Apii Ulberg - *Domestic Services*

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

PA to Director (Human Resources)

Gabrielle Dennis *RSA(English), Pitmans*

RESEARCH CONSULTANTS

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

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

Prof Brett Delahunt, *University of Otago*

Dr Michael Findlay, *Cancer Trials NZ, University of Auckland*

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

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

ADVISORS

Auditors - *Deloitte*

Bankers - *The National Bank*

Investments - *David Wale*

Solicitors - *Simpson Grierson*

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