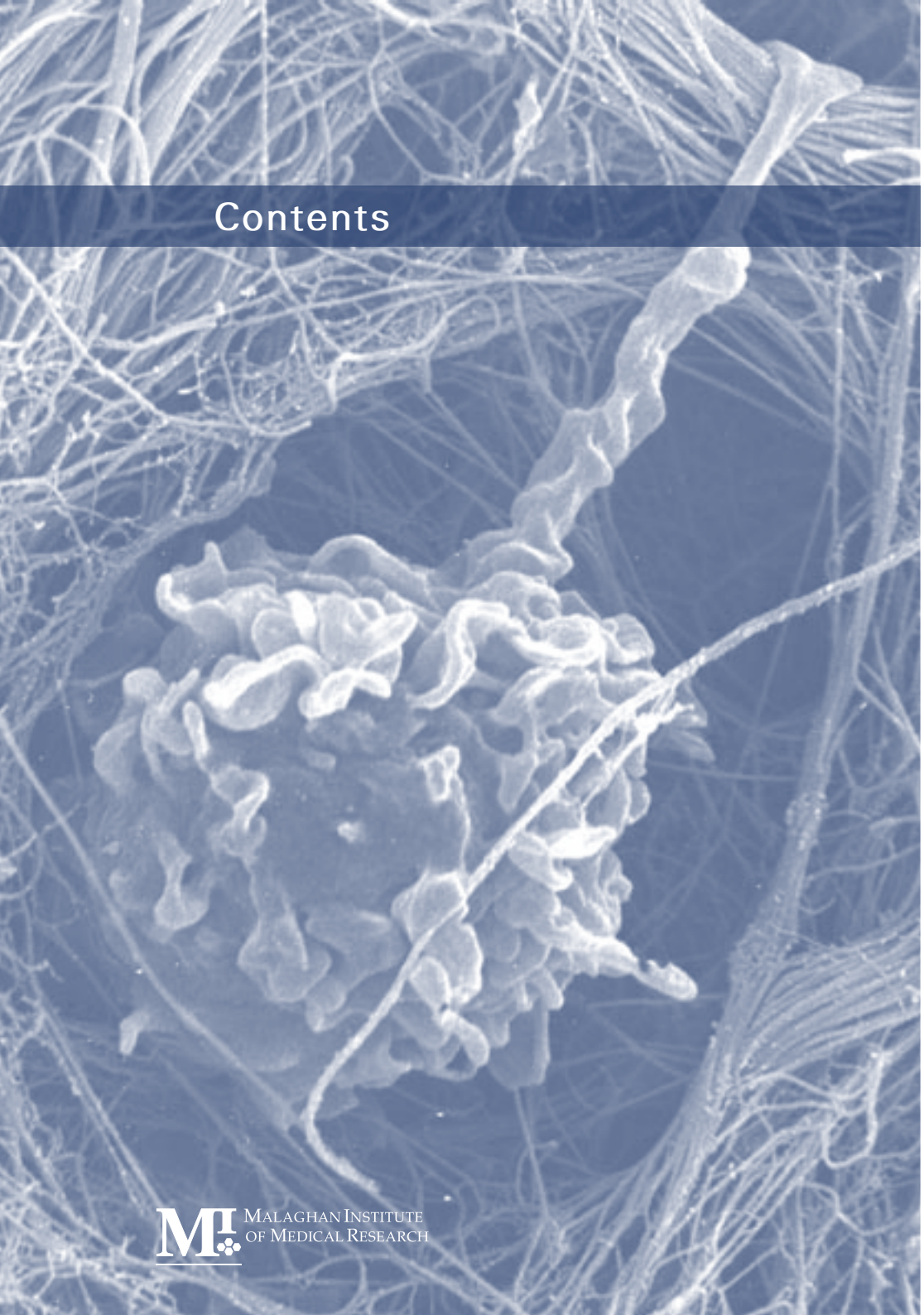
Malaghan Institute of Medical Research

Annual Report 06



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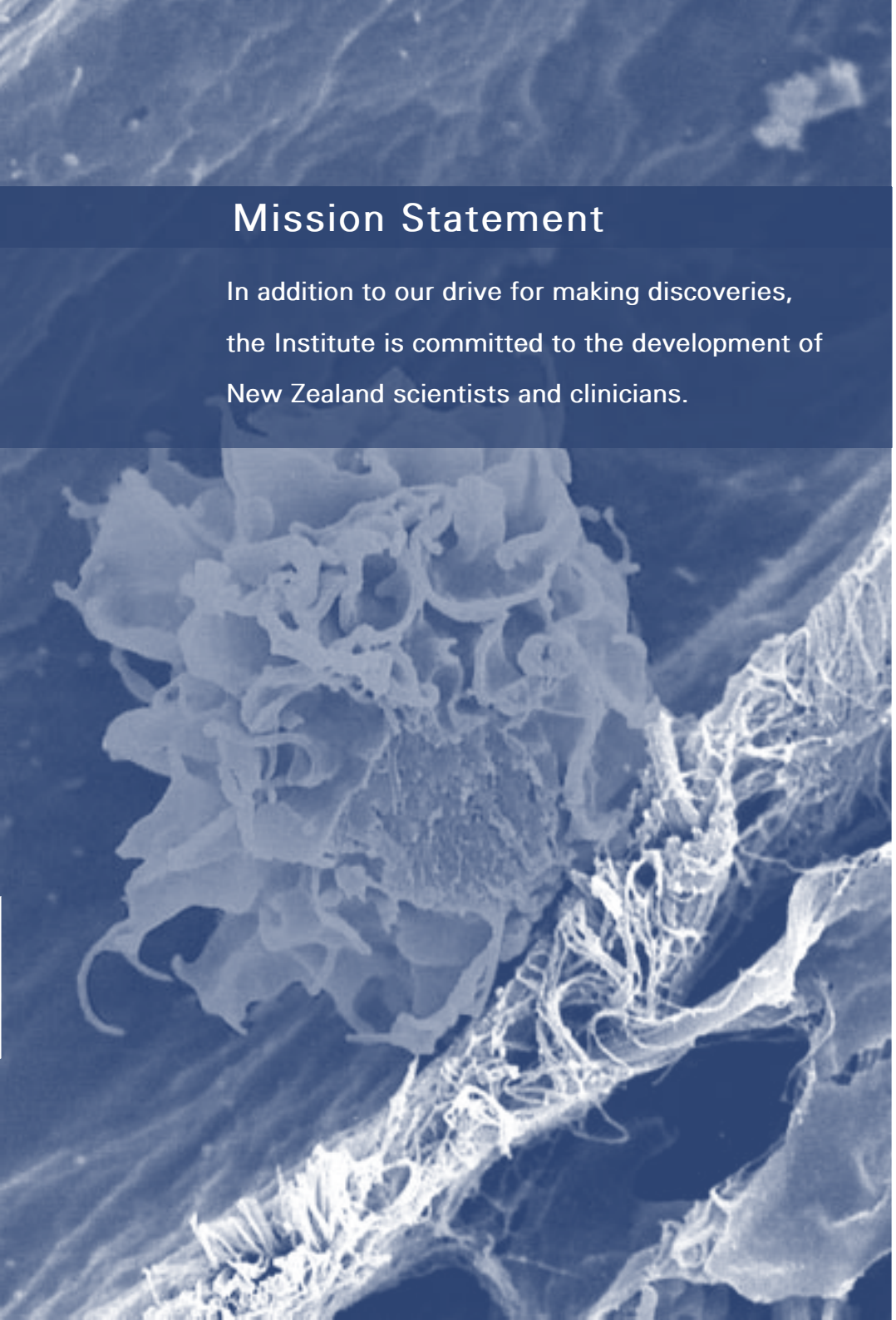


Mission Statement

In addition to our drive for making discoveries, the Institute is committed to the development of New Zealand scientists and clinicians.

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

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

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

The 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. Although completely independent, the Institute maintains close collaborative relationships with tertiary institutions, Crown Research Institutes, hospitals and clinics throughout New Zealand.

Chairman's Report

Support comes in many ways but all contribute to the whole. Donors, members of our Friends groups and Trustees all give of their time, knowledge, expertise and energy, often at considerable expense to themselves.

Malaghan Institute of Medical Research

As Chairman, I have the opportunity to head a unique organisation that has no similar peers in NZ and few worldwide.

Our scientists, both skilled and those learning, give of themselves in a way not well appreciated. We are not an institution that can offer attractive salaries or job security. The researchers themselves have to obtain the funding for their incomes and direct expenses. This is accomplished by making competitive applications for grants, almost on an annual basis. The grants are made available by Government agencies, such as the Health Research Council, or others such as the NZ Cancer Society. Competition comes from other scientists employed by the likes of Crown Research Institutes and Universities.

The ability to compete is based on the researcher's track record, which is established by having the work by their team published in an international journal that specialises in publishing original work of merit; the ranking and competition from these journals is the benchmarking. The competition for our research teams is therefore as much international as it is local.

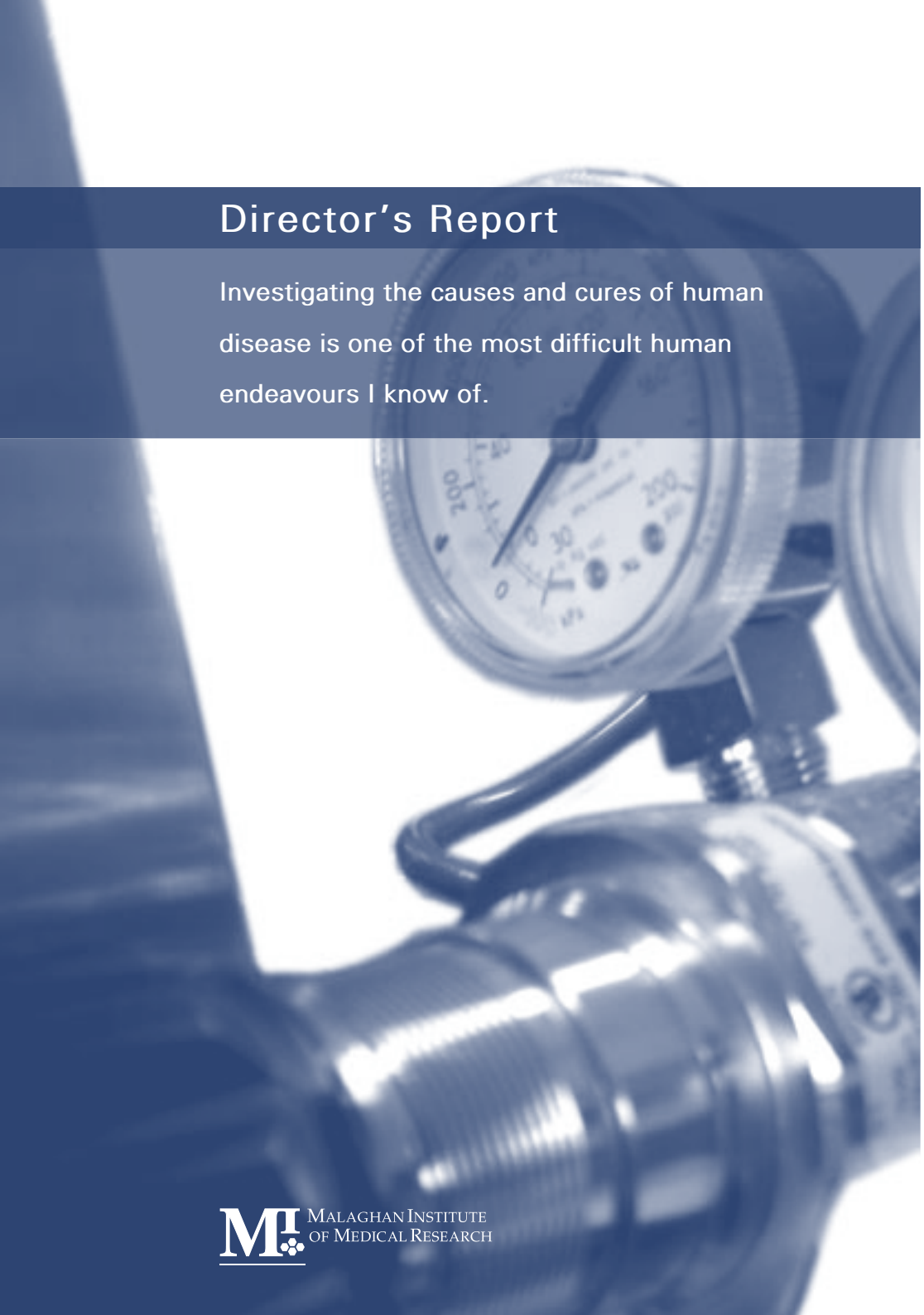
The risks of failure, by not achieving the objectives of the grant, or by being beaten to the answer by another team elsewhere in the world, will mean that they are unlikely to accomplish another grant, and thereby fund their own salary - this is an inherent risk that our researchers take. It is these pressures and challenges combined with enthusiasm and intelligence that gives our teams the real energy to succeed.

An institution such as the Malaghan has to provide the resources, environment and support functions that will attract the best researchers; it can only do so with the commitment of you and yours. Support comes in many ways but all contribute to the whole. Donors, members of our Friends groups, and Trustees all give of their time, knowledge, expertise and energy, often at considerable expense to themselves. This energy combined with that of our researchers creates a passion to succeed and to do well by our community in seeking answers to our health issues.

The Malaghan receives no direct funding from the Government, pays rent to its host University, relishes the collaborative opportunity to work with others, and therefore relies on so many individuals and groups for its ability to fund 'the tools of the trade' at the forefront of international standards, thus allowing our researchers the opportunity to succeed in their pursuit of discovery and excellence. This coming year will see Trustees focusing on funding the future.

The Director, Prof Graham Le Gros, is the driving force that grows and nurtures these unique teams of people on the journey that we are on - I salute you all...

Graham Malaghan
CHAIRMAN



Director's Report

Investigating the causes and cures of human disease is one of the most difficult human endeavours I know of.

Malaghan Institute of Medical Research

The Malaghan Institute holds a special and distinctive place in the New Zealand health research scene. The major expertise of our scientists is in the fields of cellular immunology, infectious disease, immune models of human disease and the development of immune system-based therapies and vaccines.

Through generous support and donations over the years we have established the relevant equipment and technologies necessary for cutting-edge immunology research, which now appears to be so highly relevant to many human diseases of particular relevance to New Zealanders. The information and knowledge gained from the international Genome Projects and molecular studies has paved the way for a better understanding of the various cell types in our body. Using this knowledge the biomedical research arena is now poised to make some outstanding new contributions to human health and the Institute is ready to make its very valuable and direct contribution to this process.

Although the independent status of the Malaghan Institute greatly facilitates our involvement in these endeavours, it should be acknowledged that we have very close research collaborations with all the major universities in New Zealand. The Institute also plays a key role in providing its relevant scientific expertise to many health providers, Government agencies, Crown entities and start-up entrepreneurial activities.

In reviewing the last 12 months it is clear 2006 has been a very active and exciting year with many notable achievements.

In the area of basic research discoveries Prof Franca Ronchese and her group made a number of seminal discoveries into the inner workings of dendritic cells, the sentinels of our immune system. These discoveries were published in leading international peer-reviewed journals during the year and revealed some key controls and check-points that operate on dendritic cells before they can stimulate an immune response. Prof Ronchese was further recognised for her work in this area by being a co-recipient of the inaugural James Watson Award for contributions to New Zealand Immunology.

In the clinical research arena Dr Carol Johnson at the Wellington Cancer Centre and Dr Ian Hermans and his research team have advanced and expanded the phase III human

dendritic cell vaccine trial for melanoma. This is a very serious and involved process in which a vaccine is prepared from the patient's own tissues and dendritic cells under specialised laboratory conditions. These conditions are referred to as GMP (Good Manufacturing Practice) and require extensive quality control and monitoring within the regulatory framework of Medsafe. It is a very significant achievement for both the clinical researchers at Capital Coast Health and Dr Hermans' scientific group to be able to conduct these types of trials here in New Zealand for the benefit of New Zealand patients.

A hot topic for 2006 has been stem cells; how they can be used for therapeutic purposes and their potential involvement in diseases such as cancer. This is a new research area that falls well outside mainstream support by Government agencies. Sir Roy McKenzie is widely acknowledged as one of New Zealand's leading philanthropists who seeks to inspire and support all types of worthwhile activities in our community. This year Sir Roy made a special contribution to the Malaghan Institute by establishing a Clinical Fellowship for Cancer Research held between the Institute and the Wellington Cancer Centre. This Fellowship enabled us to recruit Dr Melanie McConnell back to New Zealand from the Mount Sinai School of Medicine, New York, USA. Dr McConnell is an exciting and determined senior researcher who was able to immediately start investigations into the potential involvement of stem cells in certain forms of cancer. The key role Sir Roy makes in enabling new breakthroughs to be quickly investigated is an important element of the Institute's research successes.

It is not only the senior researchers who should be acknowledged for their research achievements in 2006. Kylie Quinn, a PhD student in the Infectious Diseases Group headed by Dr Joanna Kirman, was awarded joint runner-up in the Advancing Human Health category of this years MacDiarmid Young Scientist of the Year Awards for her work into the development of a more effective vaccine against Tuberculosis. Nicholas van Panhuys, a PhD student in my Asthma Group, was invited to speak on his research discoveries at the prestigious Keystone meeting on Allergy and Asthma, while PhD student Rachel Perret from Prof Ronchese's Cancer Immunotherapy Group, with the support of a Harry & Beverly Romanes scholarship, did a spectacular job of presenting her work to several leading international laboratories and two international conferences.

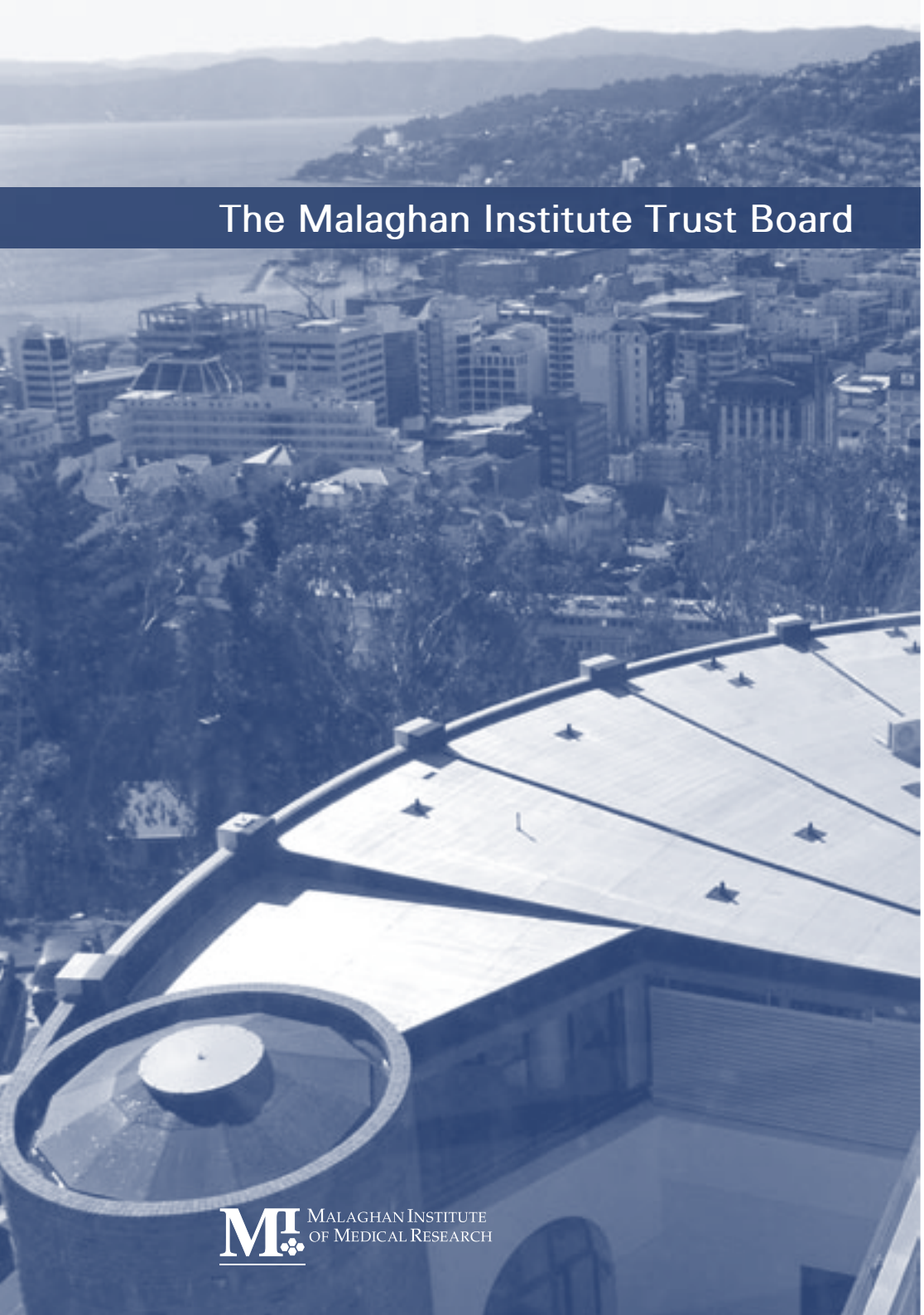
It is a privilege to be able to work with such energetic and creative young scientists and fantastic that they and their research discoveries are noticed and applauded by internationally recognised scientists.

Based on my 20 years research experience, it has to be said that investigating the causes and cures of human disease is one of the most difficult human endeavours I know of. Many of the pathological processes underlying diseases such as cancer, asthma and arthritis are complex, occur over a protracted time-frame, and are difficult to model in a simple test-tube reaction. Furthermore, many of the very sensitive techniques scientists require to dissect apart the many interacting processes are expensive, require a great deal of training, and present hazards to the researchers using them. And often the full implications of a major discovery will take decades of research to be fully proven.

I have seen how some research breakthroughs have taken decades to come to fruition as a therapy, often outliving their discoverer. What arms the scientist to either start or continue this endeavour?

I believe the key to the Malaghan Institute's success is the support of the many donors, volunteers and interested individuals who have the motivation, patience and perhaps experience of how to make a fundamental difference to our society through knowledge and the pursuit of scientific truth. In particular, I would like to take this opportunity to express my deepest gratitude to AMI for all their support this year. They and their staff have gotten right behind the Institute's research efforts into cancer and asthma. On behalf of the staff of the Malaghan Institute, I thank you all for your continuing support.

Graham Le Gros
DIRECTOR



The Malaghan Institute Trust Board

Graham Malaghan

John Beattie

John Carter

Bryan Johnson

Graham Malaghan *FCILT (Chairman)*

In 1990, was appointed as the Chairman of the Malaghan Institute. He commenced employment at General Foods Corp in 1967, was appointed General Manager of Refrigerated Freight Lines in 1970, acquiring the company in 1987. Was founding Chairman of Tasman Express Line. Was a Member of the LTSA for six years. Current directorships include several private companies, in health foods, courier services, GPS/GSM tracking devices, mineral processing and forestry facilities.

John Beattie *LLB(Victoria)*

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

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

Bryan Johnson *BCA(Victoria)*

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

Malaghan Institute of Medical Research


Graham Le Gros


John Nacey


Gary Quirke


C Dan Williams


Jim Watson


David Bibby


David H Mossman

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

Was awarded a Fogarty Fellowship at the NIH, Washington DC in 1987-1989, then took a scientist position with Ciba-Geigy in Basel Switzerland for five years before returning to New Zealand to take up the appointment as Research Director of the Malaghan Institute in 1994. Is a member of the Cancer Society's Scientific Committee, Lotteries Health Committee, Wellington Medical Research Foundation Scientific Committee, various science advisory groups, is a Professor for the Department of Biological Sciences, Victoria University, and has been elected as a Fellow of the Royal Society of New Zealand.

Prof John Nacey *MBChB, MBA, MD(Otago), FRACS*

Was appointed to the Malaghan Trust Board in 1998. Is currently the Dean of the Wellingt on School of Medicine & Health Sciences. He has clinical practice as a specialist Urologist and has had long standing research interests in benign & malignant prostate disease.

Gary Quirke *BCA, CA, FCILT*

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

C Dan Williams *CA*

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

Dr Jim Watson *PhD(Auck)*

Was appointed to the Malaghan Institute Trust Board in 1993. Until recently has been the Chief Executive of Genesis Research & Development Corporation Limited, a company he co-founded in 1994. Has held Professorships at the University of California, Irvine (1976-81) and the University of Auckland (1981-93) serving as Head of the Department of Molecular Medicine (1983–93). He was a Director of the Foundation for Research, Science and Technology (1999–2002), President of the Australasian Society of Immunology (2001), the President of the Royal Society of New Zealand (2003-2006) and a Member of the Government's Growth and Innovation Advisory Board (2001-2004).

Prof David Bibby *DSc(Loughborough University)*

Was appointed to the Malaghan Institute Trust Board in December 2004. He is currently Pro Vice Chancellor (Science), Dean of Science and Dean of Architecture and Design at Victoria University of Wellington. He holds a PhD in nuclear chemistry and was awarded a DSc in 1995. He moved to the DSIR Chemistry Division in 1975 where he became Group Manager Research before joining Industrial Research Ltd in 1992, initially as General Manager Communications, Electronics and IT and then as General Manager Science Development. In 2003, he took his present position at Victoria University of Wellington.

Dr David H Mossman *BVSc, MRCVS, MNZIF*

Graduated from the University of Queensland in 1965 with a Veterinary Degree. Awarded the Australian College of Veterinary Scientists college prize in 1978, and the Coopers NZ Farm Management Award for significant innovative farm management concepts of great relevance to pastoral farming in New Zealand in 1984. A major involvement in Beef Cattle production research and delivered Scientific Papers to the New Zealand, Australian, and British Veterinary Associations, and was Key note speaker at the World Angus and Hereford Conferences. A Member of the Lindisfarne College Board 1981-85. Managing Director of Farming, Forestry, Finance and Property Development Companies. Chairman of the Hawkes Bay Friends of the Malaghan Institute since 1999 and Retired Rural Veterinarian since 2001.

Cancer Immunotherapy

Malaghan Institute of Medical Research

Clinical Perspective and Overview of Disease

Cancer is responsible for nearly a third of all deaths in New Zealand, and has a devastating impact, both personally and financially, on individuals, families and nations worldwide. While several treatments are available, they are often ineffective at completely eradicating the disease and better therapies with fewer side effects are required. One such approach that holds great promise for cancer treatment is immunotherapy.

The concept of immunotherapy is based on the body's immune system, a network of specialised cells that protect us against diseases caused by infectious agents such as bacteria, viruses and parasites. When cells become cancerous they produce abnormal proteins not found on healthy cells that act as markers for recognition by the immune system. The immune response to cancer is not as robust as that to infectious agents such as viruses or bacteria however, because tumours arise from cells from within the body, so can often escape recognition as "foreign" by the immune system.

We are using dendritic cells, a rare population of immune cells, as the basis of cancer vaccines designed to instruct the immune system to selectively recognise and destroy cancer cells, leaving normal healthy cells unaffected.

Project One: Regulation of the Immune Response by Perforin

The ability of dendritic cells to induce immune responses and be effective cancer vaccines is dependent on their survival. We have observed that dendritic cell survival is strongly influenced by their interaction with other cells of the immune system. Some cell populations such as helper T cells improve dendritic cell survival, while interaction with cytotoxic T lymphocytes can lead to their rapid elimination.

Last year we showed that the mechanism of dendritic cell killing is perforin-dependent. Perforin is a protein produced and stored by cytotoxic T lymphocytes that is critical to the T lymphocyte's ability to kill virus infected cells and tumour cells. In 2006 we showed that elimination of dendritic cells prevents them from restimulating anti-tumour immune responses during immunotherapy. We also focused on identifying ways to extend dendritic cell survival by changing the way the cells are loaded with antigen, and better characterising where dendritic cell killing is occurring. Lastly, we started to examine whether perforin-dependent killing plays a role in regulating the survival of endogenous antigen-presenting dendritic cells, and possibly the magnitude of the immune response, during a natural infection.

Group Members

Prof Franca Ronchese, Kate Andrew (to May), Haley Ataera, Laura Green, Dr Jae Jung (to May), Rachel Perret, Jim Qin, Helen Simkins, Dr Patrizia Stoitzner, Dr Mark (Jianping) Yang

Project Two: Tumour Vaccination by Epicutaneous Immunisation

The skin is the site of an especially dense network of dendritic cells called Langerhans cells. In 2005 we showed that application of tumour antigen in a cream to the skin (epicutaneous immunisation) induced the activation of tumour-specific T cells, and that these T cells were able to attack the tumour. This work has particular relevance to the immunotherapy of skin cancers such as melanoma. This year we looked at optimising the application method using adjuvants and immune-stimulating compounds such as αGalCer that induce the activity of NKT cells.

We were also interested in identifying the immune cells present inside a tumour following an anti-tumour immune response. Using FACS analysis and staining of melanoma tumour sections we found that most of the tumour-infiltrating immune cells were macrophages, with a few dendritic cells, B cells and T cells. Although dendritic cells isolated from the tumours were shown to be functional in antigen uptake, they were not able to activate tumour-specific CD4 and CD8 T cells *in vitro*. We were however able to detect tumour antigen presenting dendritic cells in the draining lymph node.

Project Three: Effective Immune Responses against Tumours

Induction of strong, long-lasting, anti-tumour immune responses is critical to the success of cancer immunotherapy. Primary immune responses to tumours are often weak and short-lived, therefore memory T cells that can rapidly become reactivated and control tumour growth are required for lasting protection.

In 2006 we have used a melanoma model to study the anti-tumour activity of two different classes of T cells, effector and memory T cells, to determine which cells should be preferentially elicited by cancer vaccines. Effector T cells are involved in the immediate attack of an invading pathogen or cancer cell, while memory T cells do not attack immediately but are long-lasting. Our results indicate that the two populations of cells are not mutually exclusive. Effector T cells can develop into long-lived protective memory cells, that is, they can attack immediately but still be present at later stages in the immune response.

In 2007 we will focus on further elucidating the mechanism by which these T cells confer protection against tumours, as this information will provide valuable insight into improving current methods of immunotherapy.

Clinical Relevance and Future Direction

Cancer immunotherapy is an effective means with which to harness the specificity and potency of the immune system to fight cancer. Unlike chemotherapy or radiotherapy, immunotherapy is a natural treatment that uses cells from a patient's own body, and is hence a more desirable therapy for most people.

The biggest bottleneck to cancer immunotherapy at present is overcoming the mechanisms that regulate the size of the anti-tumour immune response. This is because tumours seem to use strategies similar to those used by our normal tissues to turn off immune responses and avoid spontaneous or excessive immune-mediated damage.

In the future we hope to design effective cancer vaccines that are able to safely avoid the mechanisms responsible for limiting current anti-tumour immune responses. In doing so we hope to demonstrate that cancer immunotherapy should be used alongside current mainstream cancer treatments.

Collaborators
Dr Michelle Epstein, University of Vienna, Austria
Dr Bronwyn Kivell, Victoria University of Wellington, New Zealand
Prof Niki Romani, Innsbruck University, Austria
Prof Michail Sitkovsky, Northeastern University, Boston,USA

Funding
Austrian Science Fund (FWF)
Cancer Society of New Zealand
Harry & Beverly Romanes
Health Research Council of New Zealand
New Zealand Lottery Health Research
The Royal Society of New Zealand Marsden Fund
University of Otago

Cancer Immunotherapy Lab Sponsored by:
HB Williams Turanga Trust

Vaccine Research

Clinical Perspective and Overview of Disease

The aim of the Vaccine Research group is to understand the cellular interactions involved in generating immune responses, with a particular focus on the mechanisms used to stimulate T cell activity. T cells are a very important immune cell subset that function in preventing the spread of infection by eliminating pathogen-infected cells, and can also contribute to the eradication of tumour tissue.

T cells with specificity for infected or cancerous tissues need to be "activated" in order to proliferate and migrate to the targeted tissue. Activating T cells is the responsibility of dendritic cells, the so-called "sentinels" of the immune system. On coming into contact with pathogens, dendritic cells (DCs) coordinate an effective counter-response that results in appropriately activated T cells. Dendritic cells can induce T cell responses of different sizes and quality depending on the pathogen encountered.

We are examining the molecular mechanisms that underlie this decision-making process, and using this knowledge to design more effective vaccines against diseases such as cancer.

Project One: Improving Vaccines with Compounds that Stimulate NKT Cells

NKT cells are an excellent source of the signals required for optimal activation of dendritic cells, and can thus significantly enhance vaccine-induced immune responses. Toll-like receptors (TLR) play a principle role in recognising pathogens and initiating innate immune responses. In 2006 we showed that powerful Th1 immune responses are stimulated by TLR ligands in combination with lipid compounds such as αGalCer that induce the activity of NKT cells. Furthermore, this combination of compounds induced greater anti-tumour activity than NKT cell stimuli or TLR ligands on their own. Every TLR ligand examined in combination with αGalCer provided potent stimulating activity. We are now examining the impact of one particular powerful combination of compounds on cancer, and the Th2-driven disease asthma. We have also established a collaboration with Gavin Painter at Industrial Research Limited to synthesise a series of novel lipid compounds based on the structure of αGalCer. It is hoped that some of the modified compounds will possess unique NKT cell stimulating activity that will drive immune responses particularly suited to given disease states. For example, one compound may be more suited to stimulating anti-tumour responses, while another may help prevent asthma.

Group Members

Dr Ian Hermans, Nina Dickgreber, Kathryn Farrand, Sam Gusscott, Dr Scott Harding, Dr Troels Petersen, Dr Anil Ranchord, Dianne Sika-Paotonu, Julie Walton, Catherine Wood

Project Two: Improving Dendritic Cell-based Vaccines for Cancer in a Laboratory Model

This is a new project for 2006 involving PhD student Dianne Sika-Paotonu and Research Fellow Dr Troels Petersen. The aim of this project is to increase the potency of dendritic cell stimulation by improving the way DCs are loaded with tumour antigens. Dr Petersen has shown that the standard protocol for antigen-loading of DCs is greatly improved by first transfecting the tumour cells with the TLR ligand Poly I:C (double-stranded RNA). He is currently investigating whether this mode of antigen loading works in conjunction with the stimulating power of NKT cells to drive even stronger anti-tumour immune responses.

Another approach being developed by the Vaccine Research Group to enhance the anti-tumour activity of DC-based vaccines is to combine this therapy with conventional treatments such as radiofrequency ablation (RFA). RFA is a precise, non-invasive way of heating, and thus killing, tumour tissue within a cancer patient. This creates an antigen source that can be taken up by DCs resident in the tumour following RFA treatment. Early results suggest that RFA does induce a weak immune response, and experiments are now being performed to assess whether these responses can be increased by injecting more DCs directly into the tumour.

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

The Malaghan Institute is currently involved in a clinical trial to determine the efficacy of using dendritic-cell based vaccines to treat cancer. The basic premise of the trial is simple – can we teach the immune system to both recognise and destroy cancer cells?

This is a phase III trial of a DC-based melanoma vaccine being undertaken in collaboration with Dr Chris Schmidt from the Queensland Institute of Medical Research, and Dr Carol Johnson and Associate Professor John Carter from the Wellington Cancer Centre. Tumour cells from stage III melanoma patients are used to prepare tailor-made vaccines that are then administered to the patients over the next two years. It is hoped that a total of 200 melanoma patients from New Zealand and Australia will participate in the trial over a two-year period.

In 2006 we received ethics committee approval to evaluate the possibility of using DC-based vaccines to treat glioma (brain cancer). This work, done in collaboration with Mr Martin Hunn, a neurosurgeon from Wellington Hospital, will help in the design of a future phase I trial to test the feasibility and safety of using DC vaccines in combination with standard chemotherapy for the treatment of this aggressive disease.

Clinical Relevance and Future Direction

In the future it is hoped that immunotherapy will be considered a conventional treatment that is used in combination with surgery, chemotherapy and radiotherapy to treat cancer. At present, immunotherapy as a stand-alone treatment for cancer may only be effective in a small number of patients. However, the real promise of this therapy is likely to be when it is appropriately sequenced with current 'standard' therapies. One treatment scenario would be to use surgery to debulk a tumour, radiotherapy and chemotherapy to attack disease at distant sites, and immunotherapy to mount an anti-tumour immune response against residual cancer cells. It is anticipated that the specificity and potency of immunotherapy will work in synergy with current cancer treatments, with the added advantage of reduced side-effects and minimal discomfort to the patient being treated. Designer therapies will be required for individual cancer patients because every tumour is different. Clinical trials such as the phase III trial being undertaken at the Malaghan Institute are therefore crucial to establishing whether tailor-made anti-tumour vaccines can be effective. If so, there may be exciting opportunities to incorporate these vaccines with other carefully selected treatments appropriate to a patient's particular cancer.

Collaborators

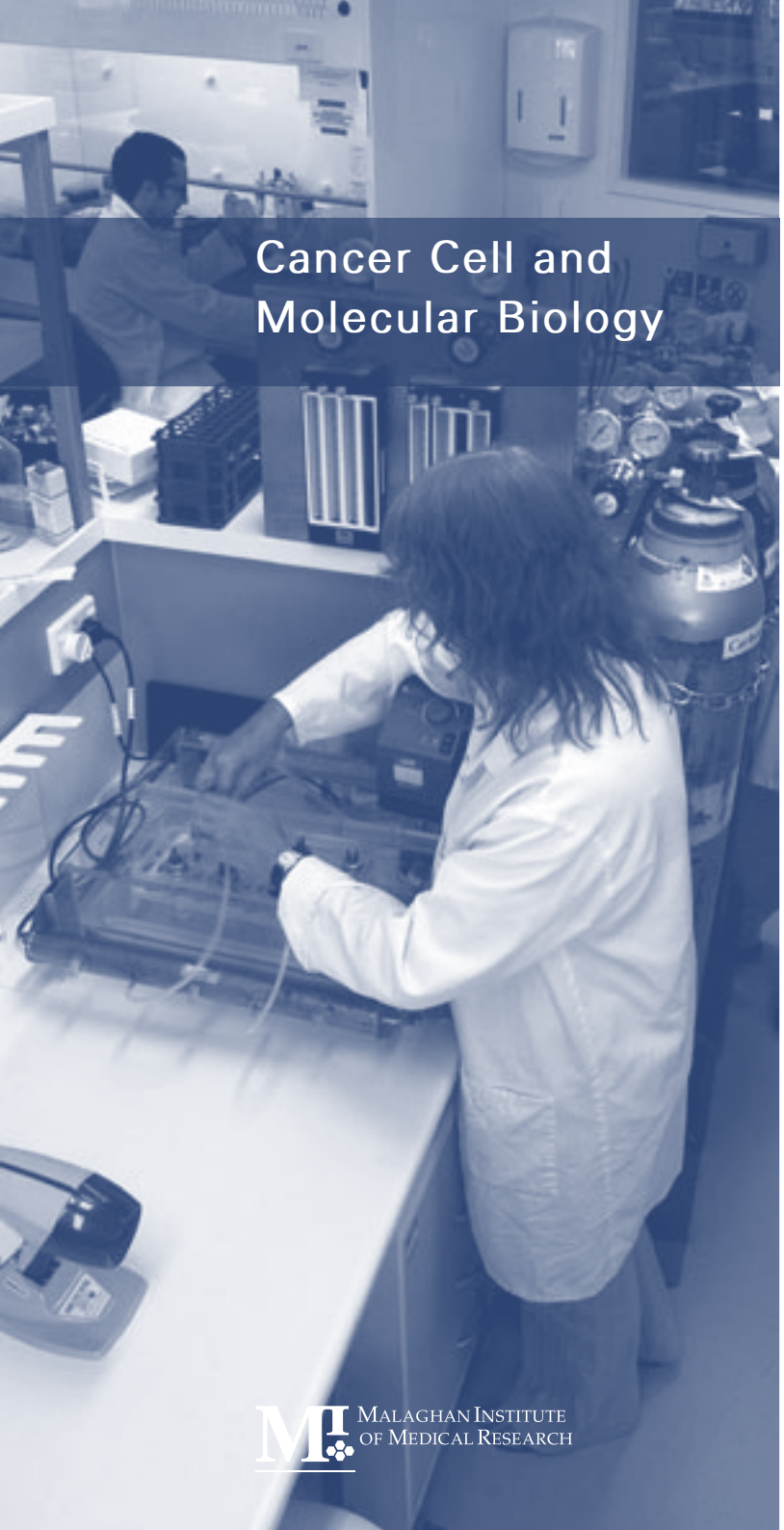
Prof Vincenzo Cerundolo, University of Oxford, UK
Dr Sarah Hook, Department of Pharmacy, University of Otago, Dunedin, New Zealand
Mr Martin Hunn, Neurosurgeon, Wellington Hospital, New Zealand
Dr Gavin Painter, Industrial Research Limited, Wellington, New Zealand
Dr Chris Schmidt, Queensland Institute of Medical Research, Australia

Funding

Health Research Council of New Zealand
Mellor Trust
Milne Trust
University of Otago
Wellington Division of New Zealand Cancer Society

Vaccine Research Lab Sponsored by:
Invitrogen

Clinical Human Immunology Lab Sponsored by:
Lion Foundation



Cancer Cell and Molecular Biology

Malaghan Institute of Medical Research

Clinical Perspective and Overview of Disease

Increasing evidence indicates that cancer is a stem cell disease involving considerable genetic change. Small populations of cancer stem cells that self-renew infrequently, give rise to rapidly-proliferating cancer cells – the target of most cancer drug development. This focus on rapidly dividing cancer cells might explain why age-adjusted cancer death rates have changed little over the past 50 years, despite an improvement in cancer remission rates and progress in developing effective cures for a small minority of cancers. Cancer stem cells are thus inherently resistant to drugs that target rapidly-dividing cells, and additionally develop multi-drug resistance.

The Cancer Cell and Molecular Biology team is developing models of cancer stem cells that will be used in drug development. Cancer cells alter their metabolism to accommodate hypoxia and nutrient limitations, and use plasma membrane electron transport (PMET) to support these changes. Our current research is aimed at developing drugs that inhibit this electron transport pathway and determining whether cancer stem cells are susceptible to drugs that compromise this energy support system.

Project One: The Cancer Stem Cell as a Target for Cancer Drug Development

If cancer stem cells underpin cancer then a cancer cure will need to address the persistence of these cells. Roy McKenzie Clinical Research Fellow, Dr Melanie McConnell, has initiated a research project aimed at developing stem cell lines from surgical glioblastoma tissue. These cell lines will be characterised and used to screen for compounds that compromise cancer stem cell survival. Dendritic cell immune responses against cancer stem cells will also be explored in collaboration with the Vaccine Research Group. We have identified and characterised a plasma membrane electron transport pathway that is essential for cancer cell proliferation and may be required for the survival of cancer stem cells that employ glycolytic metabolism. In collaboration with Professor Rob Smith, and Dr Bridget Stocker, we are building novel chemical compounds designed to insert across the outer leaflet of the cell membrane and inhibit this pathway. In another collaboration with Associate Professor Brent Copp we have mapped structure-activity relationships of 30 natural and semi-synthetic discorhabdins for their ability to block plasma membrane electron transport and cancer cell proliferation. In 2007 several of these active compounds will be modified to restrict their activity to the plasma membrane.

Group Members

Prof Mike Berridge, Dr James Baty (to Feb), Carole Grasso, Dr Patries Herst, Dr Melanie McConnell and An Tan

Collaborators

Dr David Brown, Novogen Inc, Sydney University, Australia

Assoc Prof Brent Copp, Chemistry Dept, University of Auckland, New Zealand

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

Project Two: Acute Responses to Reductive Stress and the Regulation of Gene Expression

Gene regulation occurs at several different levels within the cell. One family of regulators that coordinate nutrient stress and hypoxic responses are the sirtuins, which deacetylate histones and other non-histone proteins and consequently adaptively alter the pattern of gene expression. A subfamily of human sirtuins, exemplified by SIRT1, sense changes in the concentration of NAD+, a pyridine nucleotide cofactor required for energy metabolism. Because the NADH/NAD+ ratio is acutely regulated by plasma membrane electron transport, inhibitors of this pathway should enhance SIRT1 activity.

Dr Melanie McConnell will explore the interplay between SIRT1 and PMET in myeloid leukaemia cells and in cancer stem cell models. Dual inhibition of PMET and SIRT1 with compounds identified in Project One and with histone deacetylase inhibitors, several of which are in advanced clinical trials, should provide a potent anti-tumour cocktail with the potential to eradicate quiescent cancer stem cells in addition to rapidly-dividing tumour cells.

Project Three: The Mechanism of Action of Novogen's Anti-cancer Drug Pipeline

Novogen's anticancer drug, phenoxodiol, which is licensed to Marshall Edwards Inc, is in early Phase III clinical trials for drug-resistant ovarian cancer and is also undergoing clinical evaluation for cervical and prostate cancer. Other isoflavene compounds in Novogen's pipeline are in preclinical or early clinical trials for a range of cancers. A pilot project established that phenoxodiol inhibited PMET and the proliferation of human leukaemic cells, and that this effect was independent of mitochondrial electron transport. In subsequent contract research, we have explored the mechanism of action of three other related Novogen compounds. These second generation drugs were up to four times more active than phenoxodiol at inhibiting PMET and at least as active at inhibiting proliferation of human leukaemic cells. In contrast, primary human fibroblasts and endothelial cells were quite resistant to these compounds.

These and other results indicate that PMET is a primary target of Novogen's anticancer drugs and support our central hypothesis that inhibiting PMET will result in anti-tumour effects.

Clinical Relevance and Future Direction

Eradicating the quiescent cancer stem cell is emerging as one of the most challenging problems in the field of cancer research. This follows the demonstration that brain, breast, prostate and colon cancer, as well as the myeloid leukaemias and multiple myeloma, are diseases in which only minor stem cell populations can fully reproduce the disease. Although several candidate drugs with some preference for cancer stem cells have been identified, and gene expression profiling to identify drug targets is underway, therapeutic approaches that specifically target cancer stem cells remain a distant dream.

Our research, which aims to understand the role of plasma membrane electron transport in cancer stem cell survival and self-renewal, and to develop drugs that interfere with this pathway and treat cancer at its source, are exciting initiatives with a distinct New Zealand flavour.

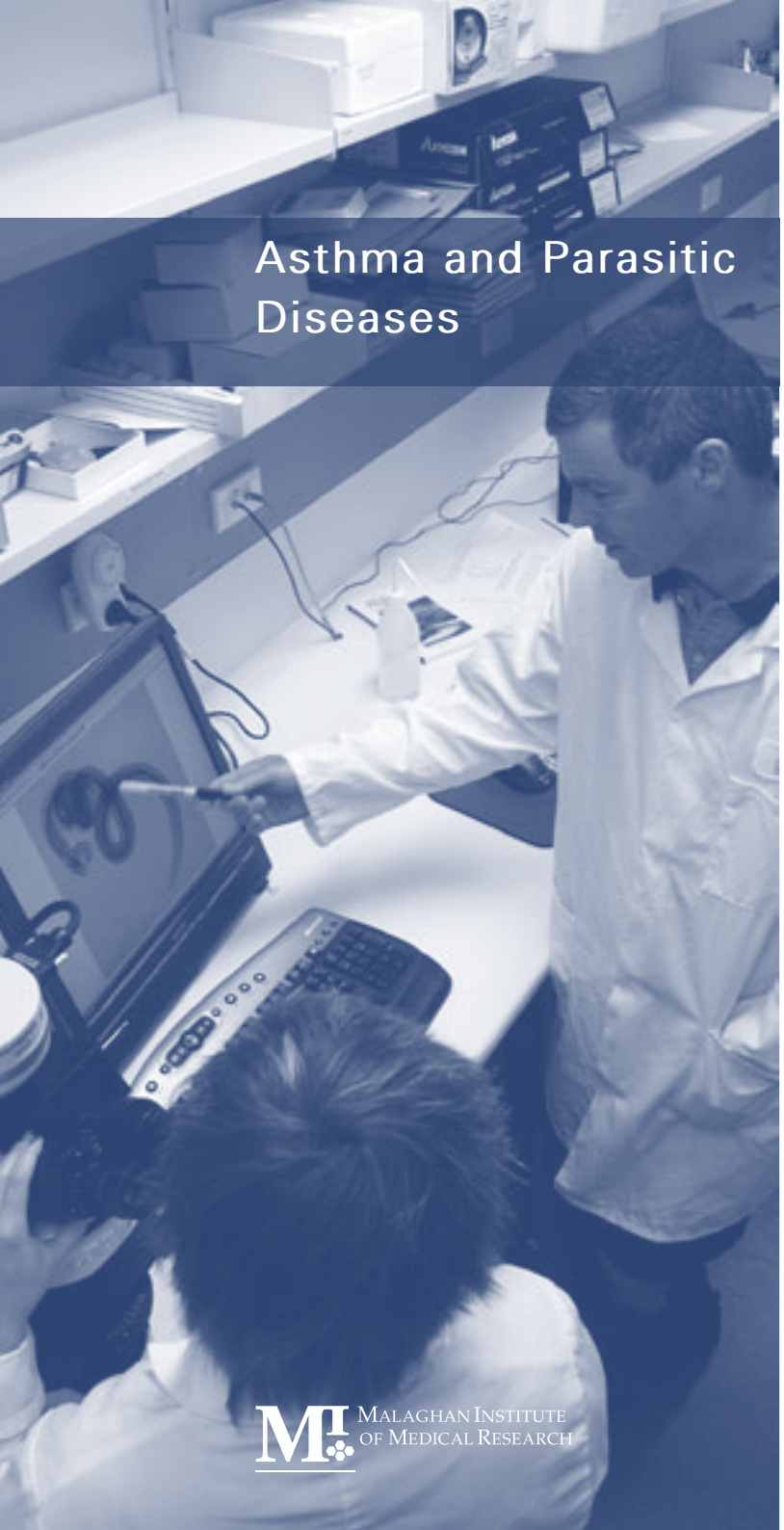
Collaborators *Cont*

Dr Pablo Etchegoin, MacDiarmid Institute, Victoria University, New Zealand
Prof Ann Smith, University of Missouri, Kansas City, USA
Prof Robin Smith, Chemistry Dept, and Dr Lesley Larsen, Crop & Food Research, University of Otago, New Zealand

Funding

Cancer Society of New Zealand
Genesis Oncology Trust
Morris Cancer Research Foundation Trust
Novogen Inc
Roy McKenzie

Cancer Cell & Molecular Biology Lab Sponsored by:
NZ Community Trust



Asthma and Parasitic Diseases

Malaghan Institute of Medical Research

Clinical Perspective and Overview of Disease

Asthma is a chronic inflammatory disease of the airways in the lungs characterised by periodic attacks of wheezing, shortness of breath, chest-tightness, and coughing. It is often triggered by harmless environmental stimulants setting off the part of the immune response (termed the Th2 immune response) that is normally involved in protecting us against parasitic worms.

New Zealand has one of the highest prevalence rates of asthma in the world; affecting one in six adults and one in five children aged 6 to 14. Hospitalisation rates for asthma sufferers have more than doubled in the past 30 years, and the condition is conservatively estimated to cost New Zealand approximately $825 million per year. Although there are treatments available that reduce the frequency and severity of asthma attacks, there is currently no cure for this disease.

We hope that by researching the underlying mechanisms of the Th2 immune response that gives rise to asthma, we will obtain the knowledge and tools necessary for the design of generally applicable vaccines and therapies for the treatment of individuals with established disease.

Project One: The Basic Biology of the Th2 Response

The cytokine interleukin-4 (IL-4) is thought to be critical for the development of Th2 CD4+ T cells that respond to parasitic infections and mediate allergic disease. We have used genetically modified mice whose Th2 cells fluoresce in a harmless way when they become active to quantify the IL-4 dependency of the Th2 immune response to the nematode parasite *Nippostrongylus brasiliensis*.

In 2006 we confirmed that IL-4 and STAT6, previously thought to be essential for inducing a Th2 immune response, were not required for Th2 development in our asthma and allergy models. IL-4 and STAT6 are however necessary for recruitment of inflammatory cells to the lung. Contrary to recent theories, we also showed that IL-2 and STAT5a signalling does not lead to Th2 induction *in vitro*.

These data indicate that the differentiation of naïve CD4 T cells to Th2 cells occurs entirely independently of IL-4 and STAT6, and that parasite and allergen challenges induce novel pathways for the selective induction of Th2 immune responses.

Group Members

Prof Graham Le Gros, Mali Camberis, Marina Harvie, Melanie Prout, Dr Debbie Scarlett (to May), Dr Bridget Stocker, Shiau-Choot Tang, Nicholas van Panhuys

Project Two: Parasites and the Th2 Response

The pathologic immune responses seen in allergic asthma are identical to the Th2 responses induced by the allergens of invading parasites or worms. This similar effect from parasites and natural allergens allows us to use parasitic worms to induce an allergic asthmatic reaction and study the mechanisms of the disease.

In 2006 we developed an Ear Model to examine the Th2 immune responses to *N. brasiliensis*. This model is a more accurate, sensitive and faster way of stimulating allergic immune responses than previous models, and is expected to provide us with true insight into how allergens/worms trigger a Th2 immune response.

We have discovered that while live worms are required to generate a systemic Th2 response, dead worms induce a strong local Th2 response in the ear and ear lymph node. In other words, a live worm infection is not required to generate a Th2 immune response. We are now using this model to screen various *N. brasiliensis* products in order to try and identify the allergenic feature(s) of the worm that causes a Th2 response.

Project Three: Synthesis of Designer Drugs Against the Bacterium that Causes Tuberculosis

In the late 1990's while searching for therapeutic ways to switch off the Th2 response, we discovered that certain types of infections actually blocked the development of asthma symptoms. One infection that has stood out in this regard is that caused by *Mycobacterium bovis*, the causative agent of Tuberculosis (Tb). We have shown that the vaccine strain of *Mycobacterium bovis*, BCG, is a safe and relatively useful way of stimulating this "protective" infection.

In 2006 we launched a spin-off project involving synthetic chemist Dr Bridget Stocker, a FRST-funded Postdoctoral Fellow, to synthesise a series of compounds that act against mycobacteria. This work will complement the Tb research of the MIMR Infectious Diseases Group. The target of these drugs is 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. We welcome Dr Stocker and the chemical analysis expertise she brings to our core asthma research programme.

Clinical Relevance and Future Direction

Asthma is a debilitating disease of major concern to our community. Our research programme is providing much needed information for the development of effective ways to treat this disease. We hope that by understanding how worm allergens stimulate the allergic Th2 immune response we will in turn learn why harmless environmental allergens can inadvertently trigger this same response. It is hoped that knowledge of such principals will aid in the design of new therapies for allergy and asthma.

A significant flip-side to our research is the identification of more effective ways to treat parasitic worm diseases. The harmless laboratory-adapted nematode we use in our studies of worm infection has similarities to parasitic worms that cause disease in humans such as the hookworm parasite. Consequently we hope to be able to use our research to make an effective vaccine that can be used to treat the many devastating parasitic worm diseases affecting humans around the world.

Collaborators

Prof Rick Maizels, University of Edinburgh, UK
Dr Kathy McCoy, University of Zurich, Switzerland
Dr Booki Min, Cleveland Clinic, USA
Dr William Paul, NIAID, National Institutes of Health, Washington DC, USA
Prof Neil Pearce, CPHR, Massey University, New Zealand
Prof Murray Selkirk, University College London, UK

Funding

AMI Insurance
Foundation for Research, Science & Technology (FRST)
Health Research Council of New Zealand
Marjorie Barclay Trust
Rex & Betty Coker Scholarship
The Royal Society of New Zealand Marsden Fund

Asthma Lab Sponsored by:
AMI Insurance

Parasitology Lab Sponsored by:
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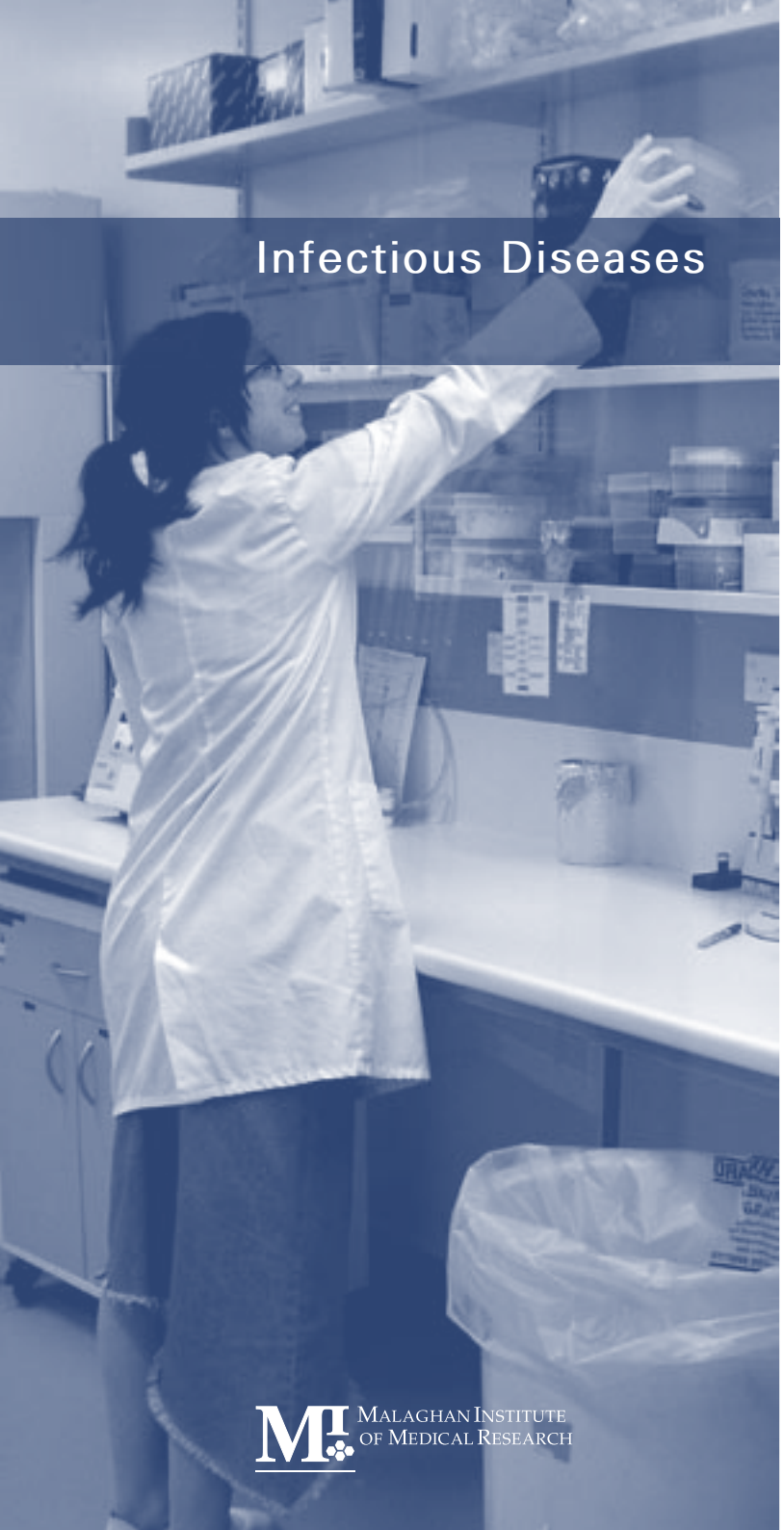


Infectious Diseases

Malaghan Institute of Medical Research

Clinical Perspective and Overview of Disease

The overall goal of the Infectious Diseases Group is to reduce the incidence of infectious disease in New Zealand through the development and implementation of vaccines. Our research focuses on three infectious microorganisms; the bacterium that causes Tuberculosis (Tb), a lung disease that kills 2-3 million people worldwide every year, and the viruses respiratory syncytial virus (RSV) and rotavirus, which cause disease in infants and the elderly.

The currently available vaccine against Tb, BCG, does not provide long-term protection against the disease. Infectious disease researchers are also faced with the challenge of disease-causing microorganisms constantly changing. It is now more evident than ever that the ability to predict and prevent future epidemics, and to develop more effective vaccines against these diseases, is vital for maintaining and improving quality of life for New Zealanders.

Studies such as those being undertaken in the Infectious Diseases Group will have important implications for vaccine design and administration.

Project One: Tuberculosis (Tb) Vaccine Development

In 2006 the news headlines were dominated by stories of Tb outbreaks. South Africa reported the largest ever outbreak of what's known as "extensively drug-resistant tuberculosis", or XDR TB, while Tb outbreaks in the Central North Island were described as the worst since the mid-1980s. Although the New Zealand outbreaks were not caused by XDR TB, the speed with which the disease spread through local communities served as a timely reminder of our need for an effective vaccine against this often overlooked disease.

The primary research focus of the Infectious Diseases Group is to understand protective immunity to the bacterium that causes Tb, and to use this information to facilitate rational design of an effective vaccine against the disease. Since individuals are exposed to multiple infectious pathogens throughout their lifetime, in 2006 we examined the effect of co-infection with other infectious organisms (such as parasites or influenza) on susceptibility to Tb. This information will enable us to predict the influence prior infection with other diseases might have on immunity against Tb following vaccination.

Group Members

Dr Joanna Kirman, Lisa Goldsack, Therése Pettersson, Kylie Quinn, Natalie Redshaw, Fenella Rich, Sophie Robinson, Catherine Wood

Collaborators

Assoc Prof Glenn Buchan, Department of Microbiology and Immunology, University of Otago, New Zealand
Drs Bryce Buddle, Geoff deLisle and Michel Denis, AgResearch, Wallaceville, New Zealand
Dr Catherine Cohet, Dodet Bioscience, Lyon, France

Collaborators *cont*

Prof Julian Crane, Clinical Epidemiology, Wellington School of Medicine, University of Otago, New Zealand
Prof Brett Delahunt, Department of Pathology, Wellington School of Medicine, University of Otago, New Zealand
Prof Keith Grimwood, Department of Paediatrics and Child Health, Wellington School of Medicine, University of Otago, New Zealand
Dr Carl Kirkwood, Murdoch Children's Research Institute, Melbourne, Australia

Project Two: Multicentre Rotavirus Strain Surveillance

Rotavirus causes greater than 50% of severe gastroenteritis in infants and young children, resulting in approximately 1000 hospitalisations in New Zealand annually.

Last year the Infectious Diseases Group established a multi-centre rotavirus strain surveillance study to monitor New Zealand's rotavirus strains pre- and post-introduction of a commercial rotavirus vaccine. Protection from infection is thought to be type-specific so it is important to understand what types of rotavirus are present in New Zealand, and how these change from year to year. Stool samples from infected infants are analysed and strain-typed at the Malaghan Institute, using molecular techniques.

An interesting finding that has come out of this study in 2006 is that the strains prevalent in the South Island in 2005/6 differed from those present in the North Island. This information will be vital for predicting the potential effectiveness of the vaccines that will be introduced to New Zealand.

Project Three: Respiratory Syncytial Virus (RSV) in New Zealand

RSV causes viral pneumonia in the elderly and bronchiolitis in young children, resulting in hospitalisation of 4% of New Zealand's infants. One of the goals of our research is to determine the reason for New Zealand's high hospitalisation rate by monitoring how RSV changes over consecutive epidemics.

Last year we showed that the two virus RSV subtypes, A and B, changed at different rates and in different ways. This will have important implications for vaccine design. In 2006 we have been analysing sample and data collections from our prospective epidemiological study (2003-2005). We have found that infants of Pacific and Maori ethnicity are more than four times as likely to be hospitalised with RSV than NZ European infants and are further examining the reasons for this.

In 2007 we will begin analysis of neutralising antibody responses to RSV infection. It is hoped that collectively this information will reveal some of the reasons behind our high hospitalisation rates for New Zealand infants with this respiratory disease.

Clinical Relevance and Future Direction

Preventing infectious disease through vaccination is the ultimate aim of the research conducted by the Infectious Diseases Group. Currently we do not have effective vaccines in New Zealand against any of the pathogens described above, nor are we assured that future vaccines created internationally will work in our unique environment.

In the future it is hoped that we will be able to identify a correlate of immune protection to expedite Tb vaccine development and testing. Without such a correlate it will take years to test each vaccine, making it even longer before we can effectively protect the New Zealand population against Tb infection.

We also hope to have identified the factors that contribute to our high RSV hospitalisation rates so that we can start looking at possible interventions to reduce the incidence of severe RSV infection in New Zealand.

Although the rotavirus vaccine is now used in many other developed countries it has yet to be approved for New Zealand and this could take years. Studies such as ours will determine whether the vaccine is likely to protect New Zealand infants against rotavirus infection.

Collaborators *cont.*

Drs Lamine Mbow and Nicole Stowell, Centocor Research & Development Incorporated, Malvern, Pennsylvania, USA
Dr Ronan O'Toole, School of Biological Sciences, Victoria University of Wellington, New Zealand
Prof Neil Pearce, Centre for Public Health Research, Massey University, New Zealand
Dr Mikhail Vyssotski, Industrial Research Ltd, Wellington, New Zealand
Dr Sarah Young, Department of Microbiology and Immunology, University of Otago, New Zealand

Also New Zealand contributions by:

Capital & Coast Health Laboratory Staff
Health Waikato
Hutt Hospital
Medlab South and Medlab Wellington
Paediatric units and laboratories at
Canterbury Health
Starship Auckland Hospital

Funding

Centocor
Health Research Council of New Zealand: Sir Charles Hercus Fellowship and Programme Grant
Merck, Sharp & Dohme NZ
New Economy Research Fund, Foundation for Research, Science & Technology (FRST)
New Zealand Lottery Health Research
University of Otago
Wellington Medical Research Foundation

Multiple Sclerosis

Malaghan Institute of Medical Research

Clinical Perspective and Overview of Disease

More than 1:1,400 New Zealanders are currently suffering from Multiple Sclerosis. It is an autoimmune disease of the central nervous system (CNS) that results in functional disability, and can render a person unable to write, speak or walk. Although so called "self-reactive T cells" (disease-causing T cells) responding to myelin components of the CNS are found in all humans, only some develop MS.

One possible reason for this is that some individuals have a malfunction in the number or function of their natural CD4+/CD25+ regulatory T cells (Tregs), a specialised immune cell type that plays a crucial role in preventing autoimmune disease. Indeed, the function of Tregs is altered in patients with MS such that they are unable to adequately turn-off disease-causing self-reactive T cells. The ultimate goal of the Multiple Sclerosis Group is to develop immunotherapeutic agents that activate Tregs for the treatment of organ-specific autoimmune diseases such as MS. We are also making use of a novel platform technology called bio-nanoparticles, to enable fast and inexpensive generation of vaccines. These particles can also be used to provide practical immunotherapy for common conditions such as cancer and autoimmunity.

Project One: Regulatory T Cells to Fight Multiple Sclerosis

Tregs have to be stimulated through their T cell receptor by peptides bound to the major histocompatibility complex (MHC) on the surface of antigen presenting cells (APCs) in order to suppress self-reactive disease-causing T cells.

Our group has exploited the activity of a modified superantigen (mSag) developed by Professor John Fraser from the University of Auckland, to deliver a myelin-derived peptide (MOG) to the immune system and stimulate Treg activity against self-reactive T cells. Superantigens are bacterial toxins with potent immune-stimulating activity that bind to the T cell receptor on T cells and the MHC molecules on APCs with high affinity.

In 2005 we showed that administration of mSag-MOG alleviated the symptoms of disease in an organ-specific experimental autoimmune encephalomyelitis (EAE) model of autoimmunity, which has similarities with human MS. The superantigen-peptide conjugate appears to do this by triggering the activation and expansion of natural regulatory T cells.

To develop this unique agent into a potential therapy, we have investigated the cellular and molecular mechanisms by which the modified superantigen-peptide conjugate activates natural regulatory T cells and inhibits autoimmunity.

Group Members

Assoc Prof Thomas Bäckström, Clare Bai, Dr Andrea McNeill (to Aug), Sara Mirmoeini, Jeanette Söederbom, Evelyn Spittle, Catherine Weir

In 2006 we showed that the modified superantigen most likely binds to a specialised APC. We hypothesise that this APC either stimulates regulatory T cells very efficiently, or is very effective in inhibiting self-reactive T cells. Currently, experiments are in place to determine which of these two possibilities is correct.

Other goals are to determine the phenotype of this APC and once identified, experiments will be conducted to evaluate the capacity of these cells to stimulate regulatory T cells *in vitro*.

Project Two: Bio-NanoParticles – A Versatile Medical Delivery Tool

Bio-nanoparticles are naturally produced 100-500 nm biopolyester particles used by many species of bacteria as a form of energy storage. These particles can potentially be engineered to deliver protein sequences that target and stimulate cells of the immune system. Such bio-nanoparticle vaccines should circumvent the toxicity and storage problems associated with live attenuated vaccines, and provide greater immunostimulatory function than current recombination vaccine strategies.

Working in collaboration with Professor Bernd Rehm from Massey University and Dr Ian Hermans, we are investigating the basic processes involved in uptake of bio-nanoparticles by APCs, and the subsequent processing and presentation of the acquired antigens to the immune system. In 2006 we successfully designed and produced bio-nanoparticles incorporating proteins that specifically target and stimulate appropriate antigen-presenting cells. The protein sequences will now be modified to create bio-nanoparticles that deliver protein antigens with enhanced activity to stimulate cells of the immune system. Ultimately the efficacy of these bio-nanoparticle generated vaccines will be assessed in disease models of influenza infection and cancer.

Clinical Relevance and Future Direction

Our immediate goal is to continue to use cell-based approaches to enhance the efficiency and number of Treg cells elicited by the modified superantigen-peptide conjugate.

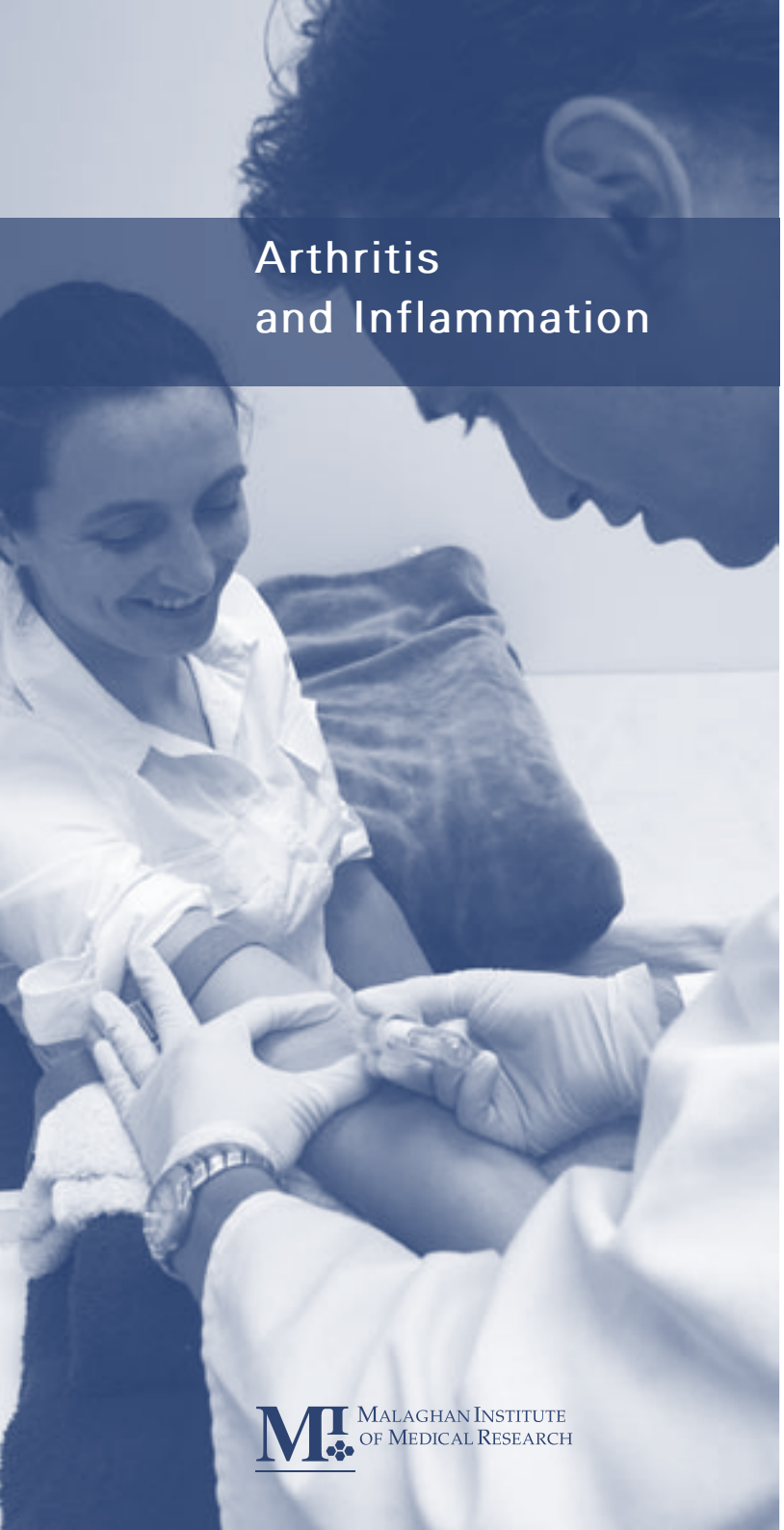
For this to be possible we need to identify the molecules, cytokines and cell types involved in this response. This information will help guide the preclinical development of the modified superantigen-peptide conjugate into a novel therapeutic agent for treating MS. If successful this technology could also be applied to other autoimmune diseases such as diabetes and arthritis.

The ease of production of vaccines using bio-nanoparticles will be a major benefit in the face of current and future global health threats such as an avian-influenza pandemic. In the long-term we hope to establish a human vaccine production centre within this country that specialises in the production of vaccines against diseases of particular relevance to New Zealanders.

Collaborators
Prof Claude Bernard, Monash University, Melbourne, Australia
Dr David Booth, Westmead Hospital, Sydney, Australia
Prof John Fraser, Auckland University, New Zealand
Prof Bernd Rehm, Massey University, New Zealand
Dr Ian van Driel, University of Melbourne, Australia

Funding
Health Research Council of New Zealand
Neurological Foundation
New Zealand Lottery Health Research
The Royal Society of NZ Marsden Fund
Wellington Medical Research Foundation

Multiple Sclerosis Lab Sponsored by:
The Wellington Company



Arthritis and Inflammation

Malaghan Institute of Medical Research

Clinical Perspective and Overview of Disease

Arthritis is often thought of as a single disease but it is actually a term used to describe over 140 inflammatory diseases that affect the musculoskeletal system or joints. Arthritis-related problems include pain, stiffness, inflammation and joint weakness, which can cause difficulties with basic daily tasks such as walking, driving a car or preparing food.

Over a quarter of New Zealand's population will develop arthritis at some stage in their lives and it is wrong to think that the disease only affects the elderly. In fact in New Zealand there are over 1000 children and young people under the age of 20 years affected by arthritis at any one time. Last year the economic and social cost of arthritis in New Zealand was estimated to be $2.56 billion in suffering and premature death.

The goal of the Arthritis Group is to identify the factors involved in the onset, duration and resolution of inflammation during an arthritic attack. This will lead to the development of new treatments for the underlying cause of the disease, including ways to identify susceptibility to inflammation in arthritis sufferers.

Project One: Role of Macrophages and Monocytes in Acute Arthritis

Gout is a painful type of arthritis that affects a great number of New Zealanders, particularly middle-aged men, Maori and Pacific Islanders. The inflammation associated with this disease is triggered by the formation of uric acid (MSU) crystals in and around the joints.

Macrophages and monocytes are recruited to joints and connective tissues in a variety of arthritic diseases. We are investigating the involvement of discrete subpopulations of these immune cells in the early stages of gouty inflammation.

In 2006 studies focused on the role of monocytes entering the site of inflammation showed that they contribute little to the initiation and progression of inflammation induced by MSU crystals, indicating that the key inflammatory cells are to be found at the site of the inflammatory insult. This finding will be followed up in 2007 to identify which cells are responsible for producing the initial inflammatory molecules, and their role in recruiting other cells that exacerbate the disease.

Project Two: A Clinical Study of Gouty Arthritis

In 2006 a qualified Rheumatologist specialising in the care of people with arthritis and inflammatory conditions, Dr Rebecca Grainger, joined the Arthritis Group to undertake her PhD studies. Dr Grainger brings extensive clinical expertise to the group, enabling us to launch a clinical study into gouty arthritis.

The goal of the clinical study is to characterise the inflammatory responses of immune cells isolated from the blood of healthy volunteers and arthritis patients, following exposure to MSU crystals (the causative agent of gouty arthritis). This study will enable us to identify any differences in the inflammatory responses between healthy patients and those with gout that may predict the onset or progression of gouty arthritis.

The clinical study complements our basic research programme investigating the mechanisms of inflammation during the early onset of arthritis and provides a clinical link to our TerraMarine Pharmaceuticals anti-inflammatory drug discovery programme.

Project Three: New Anti-inflammatory Treatments for Arthritis

In collaboration with the National Institute of Water and Atmospheric Research (NIWA), and Crop & Food Research, we have progressed our TerraMarine programme to discover novel anti-inflammatory compounds from New Zealand biota. This programme aims to inhibit the production of damage causing superoxide by neutrophils at the site of inflammation.

The first compound in our development pipeline is undergoing the final stages of chemical modification aimed at improving solubility and bioavailability *in vivo*. The best synthetic candidate will then be moved forward into preclinical studies in 2007. A second novel compound has also been identified with the potential to enter the development pipeline.

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

Clinical Relevance and Future Direction

Over the coming years we would like to expand our basic research programme to include other arthritic and inflammatory diseases.

We would also like to develop a greater interface with the clinic to set up more clinical trials into inflammatory disease.

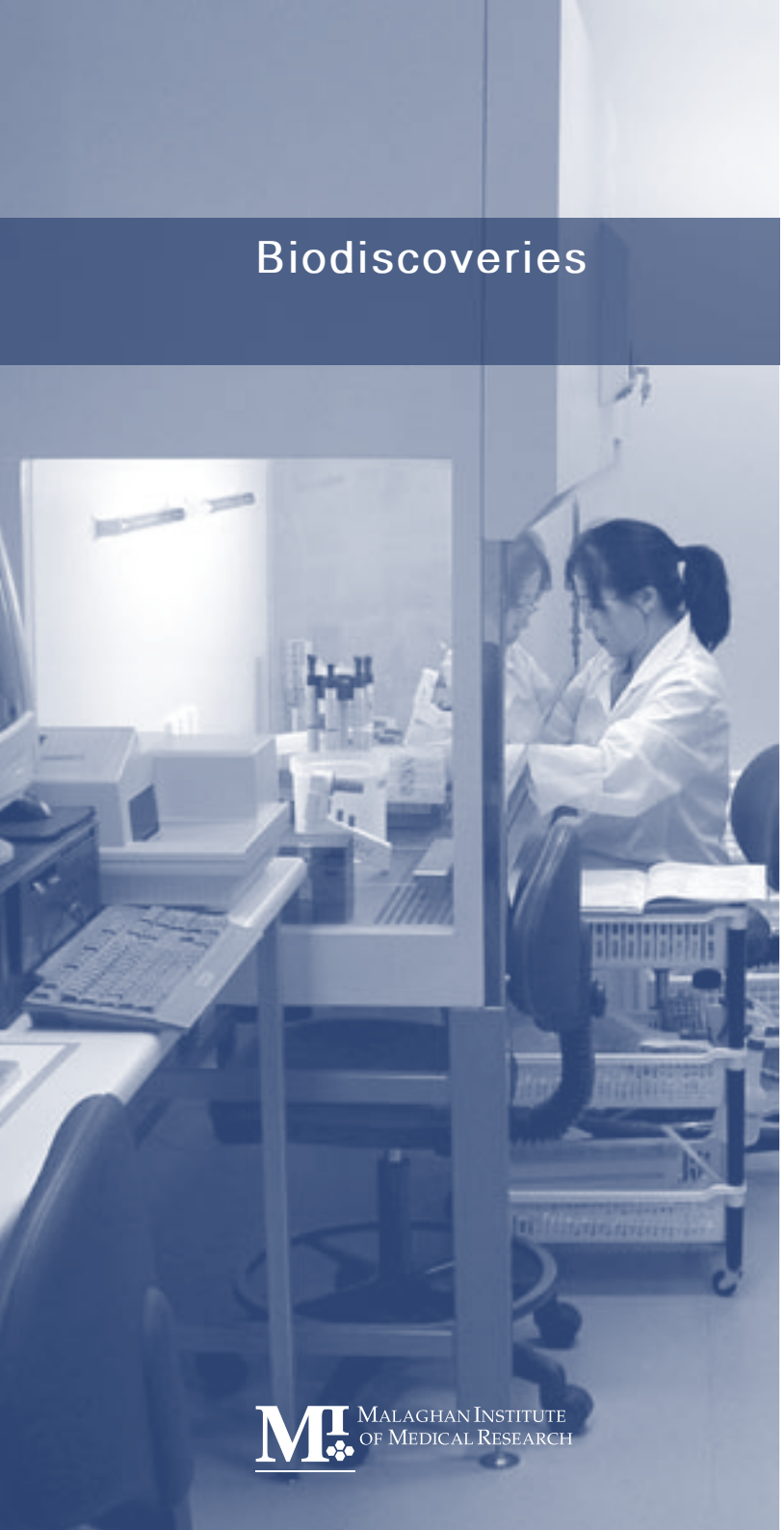
Finally, we hope to be able to use our basic research findings to identify new targets for disease therapy that can be taken into drug development.

Group Members
Dr Jacquie Harper, Elizabeth Chia, Oliver Chow Worn (to Nov), Dr Rebecca Grainger, William-John Martin, Rene McLaughlin

Collaborators
Dr Brent Copp, Auckland University, New Zealand
Dr Lindsay Dent, Adelaide University, Australia
Dr Andrew Harrison, Wellington School of Medicine, New Zealand
Dr Nigel Perry, Crop and Food Research, New Zealand
Dr Vicky Webb, NIWA, New Zealand

Funding
Foundation for Research, Science & Technology (FRST)
Health Research Council of New Zealand
New Zealand Lottery Health Research

Biodiscoveries



Malaghan Institute of Medical Research

Clinical Perspective and Overview of Disease

The biodiversity of New Zealand's marine and terrestrial organisms represents huge potential for the identification of novel bioactive molecules for drug development. Natural remedies have been used for centuries and about half the drugs on the market today originally came from natural sources. Some of the most well-known examples include aspirin from willow bark, penicillin from mould and taxol from the yew tree. This unique resource is being targeted by TerraMarine Pharmaceuticals, a joint venture between the Malaghan Institute of Medical Research, Crop & Food Research, and the National Institute of Water and Atmospheric Research (NIWA).

Formed in 2002, the focus of this collaboration is the identification of molecules from New Zealand's unique plant and marine life that possess anti-inflammatory activity. These compounds will then form a starting point from which potential drug leads can be developed.

Initial research will target identification of novel non-steroidal anti-inflammatory drugs (NSAIDs), an area of rapid growth as the average age of global populations, and hence the need for drugs to treat age-related inflammatory diseases such as arthritis, continues to rise.

Sample Collection

New Zealand's land and surrounding seas provide a rich hunting ground for new medicinal compounds. NIWA divers collect and store samples from a wide variety of marine plants and animals including fish, shellfish, sponges, sea squirts and seaweeds. Crop & Food Research provides a complementary collection of terrestrial plant samples.

The flora and fauna samples collected by NIWA or Crop & Food Research can potentially contain several hundred different chemicals. After they have been classified, catalogued and dissected back in the laboratory, extracts prepared from the samples are given to the Malaghan Institute to be put through a series of screens to see which, if any, possess anti-inflammatory properties.

Target Assays

The Malaghan Institute Biodiscoveries Group uses a medium-throughput human microplate assay to screen New Zealand biota for novel anti-inflammatory activity. The target of this assay is the human neutrophil respiratory burst.

Neutrophils constitute the "first line of defence" against infectious agents such as bacteria or fungi that penetrate the body's physical barriers. Upon activation neutrophils have increased oxygen consumption, a process known as the respiratory burst, in which they produce reactive oxygen species to attack the invading pathogens. In diseases such as arthritis or asthma however, the neutrophil inflammatory response goes unchecked and damages rather than protects the body's cells and tissues.

If a molecule is shown to inhibit the neutrophil respiratory burst, it is then screened for its ability to halt neutrophil inflammation in a murine model of gout that aligns well with the human clinical disease. This information is then used in combination with toxicity studies to determine whether or not the compound will be progressed through to clinical trial.

The Lead Compounds

We have identified several lead compounds that both inhibit the activity of the human neutrophil respiratory burst and suppress neutrophil infiltration in murine models of inflammation.

The first compound in our development pipeline is undergoing the final stages of chemical modification aimed at improving solubility and bioavailability *in vivo*. A second novel compound has also been identified with the potential to enter the development pipeline.

The best synthetic candidate from our development programme will be moved forward into preclinical studies in 2007.

Clinical Relevance and Future Direction

Inflammation is a common underlying factor contributing to the exacerbation of a wide variety of disease states including arthritis, asthma, and cardiovascular disease.

Many of these diseases involve the recruitment of neutrophils and due to over production of superoxide, damage of surrounding tissues. As a result, anti-inflammatory drugs targeting neutrophil recruitment and activity would have a wide application in the treatment of inflammatory disease.

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

Group Members

Dr Jacquie Harper, Elizabeth Chia, Oliver Chow Worn (to Nov), Dr Rebecca Grainger, William-John Martin, Rene McLaughlin

Collaborators

Dr Brent Copp, Auckland University, New Zealand
Dr Lindsay Dent, Adelaide University, Australia
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Funding

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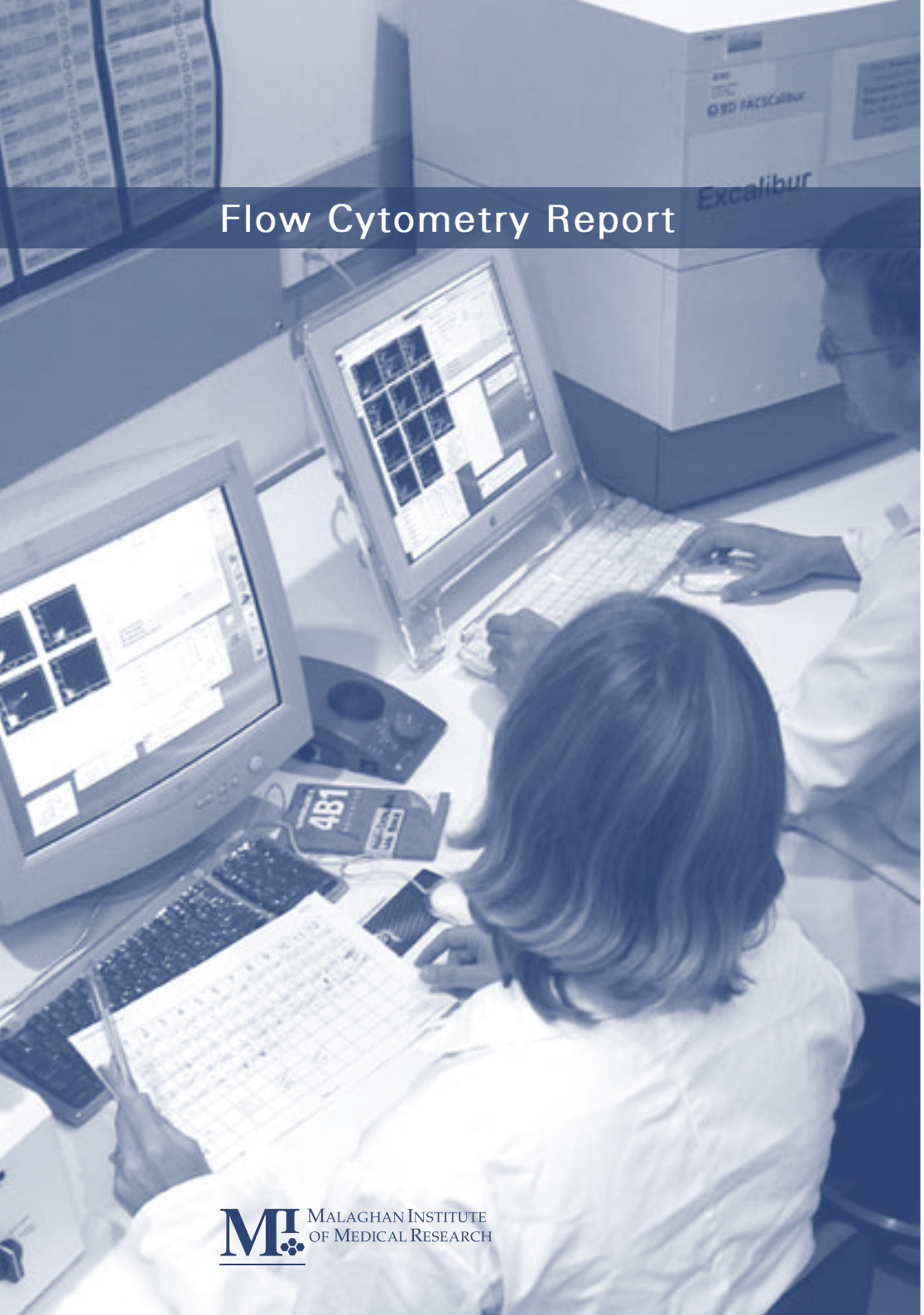

Flow Cytometry Report

Malaghan Institute of Medical Research

Flow cytometry is the cornerstone technique for cell analysis at the Malaghan Institute, and we are the busiest research-based flow cytometry laboratory in New Zealand with state-of-the-art cytometers.

Fluorescence-activated flow cytometry is one of the most powerful technologies used in immunology research and works by utilising lasers to excite fluorescent dyes attached to specific cell types. This enables recognition and sorting of cells of interest. My role as flow cytometrist is to offer support and information to the researchers regarding new fluorophores, dyes or technologies that will benefit their experimentation. I also maintain all the Flow Suite equipment so that everything runs smoothly. My position is unique as my role is one of only two at this level in New Zealand.

One of the most vital pieces of equipment that we rely on for all our experiments is the BD FACSVantage DiVa, a large flow cytometer equipped with cell sorting capabilities. Cells are inserted into the flow cytometer in a fluid stream that is broken up into droplets by vibration of the nozzle they come out of. If a droplet contains a cell-type of interest, it gets electronically charged and deflected into a collection vessel by passage through an electric field.

With our FACSVantage DiVa I can analyse up to 10,000 individual cells per second, looking at five different markers and two physical properties of how each cell scatters light to allow the identification and sorting of often very small populations of cells.

Two projects that have kept me particularly busy this year have been with the Infectious Diseases and Cancer Immunotherapy research groups, where I have been involved in sorting memory T cells that are reactive against Tuberculosis, and in isolating dendritic cells from tumours to see if they can induce anti-tumour immune responses.

A key research initiative is the need to develop the skills and techniques to sort cancer stem cells. These very rare cells have been an overlooked issue in cancer treatment and cancer cell drug targeting. However there are obvious dangers in working with stem cells and the powerful UV laser that is used to identify them. We feel very privileged to receive the support of AMI who understood the importance of us undertaking this research and made a generous donation that enabled us to purchase a new UV laser that

will allow sorting of these cells and construction of an aerosol containment system to ensure the process is completely safe. This equipment allows us to now rapidly pursue groundbreaking investigations into the true origins of cancer and its causes.

The Flow Suite also acquired a Bio-Rad suspension array plate-reader in 2006 that allows researchers to analyse up to 100 different biomolecules within a single drop of sample.

Our future direction will be to have the cancer stem cell sorting up and running and to work towards purchasing another benchtop analyser in 2008. The new benchtop analyser will allow analysis of up to 18 different fluorophores simultaneously, compared to our current benchtop cytometers that can only analyse four colours.

The Malaghan Institute Flow Cytometry Suite is running at full capacity at the moment and the future for this lab is very bright and very busy.

Kylie Price
FLOW CYTOMETRY SUITE MANAGER

Publications

Ainge GD, Hudson J, Larsen DS, Painter GF, Singh GD, Harper JL (2006) Phosphatidylinositol mannosides: synthesis and suppression of allergic airway disease. **Bio-organic & Medicinal Chemical Letters** 14: 5632-5642

Copp BR, Pearce AN, Denny WA, Berridge MV, Harper JL, Perry NB, Larsen L, Godfrey CA. "Anti-inflammatory compounds". **Patent** PCT/NZ2005/000246, published as WO06/031134 on 23 March 2006

Daly JW, Camerini-Otero C, Shapiro CA, Ma J, Ziffer H, Velex L, Harper JL (2006) Further studies on the interaction of loperamide with capacitative calcium entry in leukemic HL-60 cells. **Drug Development Research** (in press)

Dupasquier M, Stoitzner P, Wan H, Cerqueira D, van Oudenaaren A, Voerman JSA, Denda-Nagai K, Irimura T, Raes G, Romani N, Leenen PJM (2006) The dermal microenvironment induces the expression of the alternative activation marker CD301/mMGL in mononuclear phagocytes, independent of IL-4/IL-13 signaling. **Journal of Leukocyte Biology** 80: 838-849

Grimwood K, Huang QS, Cohet C, Gosling IA, Hook SM, Teele DW, Pinnock RE, Nicholson WR, Graham DA, Farrell AP, Leadbitter P, Lennon DR (2006) Rotavirus hospitalisation in New Zealand children under three years of age. **Journal of Paediatric Child Health** 42: 196-203

Harper JL, Larsen D, Severn W, Singh G "Synthetic molecules having immune activity", NZ 529603/533245, **Patent** Acceptance, December 2006

Hermans IF, Silk JD, Gileadi U, Masri SH, Shepherd D, Farrand KJ, Salio M, Cerundolo V (2006) DC function can be modulated through the cooperative actions of toll-like receptor ligands and invariant NKT cells. **Journal of Immunology** (in press)

Herst PM, Berridge MV (2006) Cell Surface Oxygen Consumption: A major contributor to cellular oxygen consumption in glycolytic cancer cell lines. **Biochemica et Biophysica Acta: Bioenergetics** (in press) [epub ahead of print Dec 6 2006]

Herst PM, Berridge MV (2006) Plasma membrane electron transport: a new target for cancer drug development. Invited Review. **Current Molecular Medicine** 8: 895-904

Herst PM, Tan AS, Berridge MV (2006) The cell membrane as a target for cancer drug development: leukaemia cell survival and growth depends on plasma membrane electron transport (PMET). **Experimental Hematology** 34: 67

La Flamme AC, Harvie M, McNeill A,Goldsack L, Tierney JB, Bäckström BT (2006) Fcgamma receptor-ligating complexes improve the course of experimental autoimmune encephalomyelitis by enhancing basal Th2 responses. **Immunology & Cell Biology** 84: 522-529

Malaghan Institute of Medical Research

Lee A, Farrand KJ, Dickgreber N, Hayman CM, Jürs S, Hermans IF, Painter GF (2006) Novel synthesis of α-galactosyl ceramides and confirmation of their powerful NKT cell agonist activity. **Carbohydrate Research** 341: 2785-2798

Liu X, Stocker BL, Seeberger PH (2006) Total synthesis of phosphatidylinositol mannosides of *Mycobacterium tuberculosis*. **Journal of the American Chemical Society** 128: 3638-3648

Matheson JW, Rich FJ, Cohet C, Grimwood K, Huang QS, Penny D, Hendy MD, Kirman JR (2006) Distinct patterns of evolution between respiratory syncytial virus subgroups A and B from New Zealand isolates collected over thirty-seven years. **Journal of Medical Virology** 78: 1354-1364

Matthews KE, Hermans IF, Roberts JM, Ching L-M, Ronchese F (2006) DMXAA treatment of a non-immunogenic tumor does not facilitate T cell priming or improve the effect of active or passive T cell immunotherapy. **Immunology & Cell Biology** 84: 383-389

Matthews KE, Karabeg A, Roberts JM, Saeland S, Dekan G, Epstein MM, Ronchese F (2006) Long-term deposition of inhaled antigen in lung resident CD11b-CD11c+ cells. **American Journal of Respiratory Cell & Molecular Biology** (in press) [epub ahead of print Nov 22 2006]

Min B, Le Gros G, Paul WE (2006) Basophils: A potential liaison between innate and adaptive immunity. Review Article. **Allergology International** 55: 99-104

Ohta A, Gorelik E, Prasad S, Ronchese F, Lukashev D, Wong M, Huang X, Caldwell S, Liu K, Smith P, Chen JF, Jackson E, Apasov S, Abrams S, Sitkovsky M (2006) A2A adenosine receptor protects tumors from antitumor T cells. **Proceedings of The National Academy of Sciences (USA)** 103: 1132-1137

Quinn KM, McHugh RS, Rich FJ, Goldsack LM, de Lisle GW, Buddle BM, Delahunt B, Kirman JR (2006) Inactivation of CD4+CD25+ regulatory T cells during early mycobacterial infection increases cytokine production but does not affect pathogen load. **Immunology & Cell Biology** 84: 467-474

Ritchie DS, Yang J, Walton J, Hermans IF, Carter J, Findlay M, Dady PJ, Rawson P, Ronchese F (2006) Autologous dendritic cells pulsed with eluted peptide as immunotherapy for advanced B-cell malignancies. **Leukemia & Lymphoma** 47: 675-682

Romani N, Ebner S, Tripp CH, Flacher V, Koch F, Stoitzner P (2006) Epidermal Langerhans cells - changing views on their function *in vivo*. **Immunology Letters** 106: 119-125

Romani N, Tripp CH, Ratzinger G, Heufler C, Koch F, Saeland S, Stoitzner P (2006) Epidermal Langerhans Cells. In **Handbook of Dendritic Cells, Biology, Diseases and Therapies**, ed. Lutz MB, Steinkasserer A, Romani N. Wiley-VCH, Weinheim, New York pp.73-100

Schröder JM, Reich K, Kabashima K, Liu FT, Romani N, Metz M, Kerstan A, Lee PHA, Loser K, Schön MP, Maurer M, Stoitzner P, Beissert S, Tokura Y, Gallo RL (2006) Who is really in control of skin immunity under physiological circumstances – lymphocytes, dendritic cells, or keratinocytes? Controversies Article. **Experimental Dermatology** 15: 913-929

Stocker BL, Hoberg JO (2006) Synthesis of platinacyclobutanes bearing biological components for targeted cisplatin prodrugs. **Organometallics** 25: 4537-4541

Stocker BL, Hölemann A, Seeberger PH (2006) Synthesis of a core arabinomannan oligosaccharide of *Mycobacterium tuberculosis*. **Journal of Organic Chemistry** 71: 8071-8088

Stoitzner P, Tripp CH, Eberhart A, Price KM, Jung JY, Bursch L, Ronchese F, Romani N (2006) Langerhans cells cross-present antigen derived from skin. **Proceedings of the National Academy of Sciences (USA)** 103: 7783-7788

Timmer MSM, Stocker BL, Seeberger PH (2006) De-novo synthesis of an aceric acid building block. **Journal of Organic Chemistry** 71: 8294-8297

Watt V, Ronchese F, Ritchie DS (2006) Resting B lymphocytes suppress tumour immunity via an MHC class-II dependent mechanism. **Journal of Immunotherapy** (in press)

Weir C, McNeill A, Hook S, Harvie M, La Flamme AC, Le Gros G, Bäckström BT (2006) Critical role of preproenkephalin in experimental autoimmune encephalomyelitis. **Journal of Neuroimmunology** 179: 18-25

Yang J, Huck S, McHugh R, Hermans I, Ronchese F (2006) Perforin-dependent elimination of dendritic cells regulates the expansion of antigen-specific CD8+ T cells *in vivo*. **Proceedings Of The National Academy Of Sciences (USA)** 103: 147-152

Seminars

January

Marie Powell, Health and Safety Nurse, Victoria University of Wellington, New Zealand. Treatment and prevention of occupational overuse syndrome.

February

Dr Merilyn Hibma, Department of Microbiology & Immunology, University of Otago, New Zealand. Human papillomaviruses and immunity: two sides of the coin.

Willy-John Martin, Malaghan Institute of Medical Research. Redoubtable Gout! Crystals are a pain.

Dr Ernest Hamel, National Cancer Institute, NIH, Bethesda, United States of America. Colchicine Site Agents.

Assoc Prof Margaret Baird, Department of Microbiology & Immunology, University of Otago, New Zealand. Workshop: An update of research in the Vaccine Group, Department of Microbiology & Immunology.

March

Prof Diane Jelinek, Mayo Clinic College of Medicine, United States of America. Malignant B cell biology: from BCR to BAFF.

Group leaders, Malaghan Institute of Medical Research. Research overview.

Dr Seumas McCroskery, Laboratory of Cell Biology, NHLBI, NIH, Bethesda, United States of America. Transmembrane agrin: "Rogaine" for neurons.

Nicholas van Panhuys, Malaghan Institute of Medical Research. Rewriting the paradigm on IL-4/Stat-6 and Th2 immunity: new rules for *in vivo* commitment?

April

Stephanie Huck, Malaghan Institute of Medical Research. Animal handling techniques.

Goetz Liable, Senior Scientist Reproductive Technologies Group, AgResearch, Ruakura, New Zealand. Biopharming in dairy cattle: production of recombinant myelin basic protein in milk.

May

Helen Simkins, Malaghan Institute of Medical Research. Immune responses in perforin-deficient mice.

Dr Patrizia Stoitzner, Malaghan Institute of Medical Research. How to use the skin immune system for cancer immunotherapy?

Prof Franca Ronchese, Prof Mike Berridge, Prof Graham Le Gros and Assoc Prof Thomas Bäckström, Malaghan Institute of Medical Research. Conference reports.

June

Dr Michel Denis, AgResearch, Wallaceville, New Zealand. Macrophages and dendritic cells in bovine tuberculosis: Thor's hammer or Trojan horse?

Dr Chris Schmidt, Head of Cancer Immunotherapy Laboratory, Queensland Institute of Medical Research, Australia. Metastatic melanoma: a model for response to immunotherapy.

Dr John Miller, School of Biological Sciences, Victoria University of Wellington, New Zealand. The peloruside diaries.

July

Dr Roslyn Kemp, National Institute for Medical Research, MRC, United Kingdom. Generation and maintenance of memory CD8+ T cells.

Rod Stewart, Quantum Scientific, Australia. Western blotting: common problems and solutions.

Prof Bruce Baguley, Medical & Health Sciences, University of Auckland, New Zealand. Tumour stem cells: implications for cancer treatment.

Dr Steven Gieseg, School of Biological Sciences, University of Canterbury, New Zealand. Macrophage antioxidants as determinates of atherosclerotic plaque formation.

Dr Roger Hurst, Senior Scientist, HortResearch Ltd, Hamilton, New Zealand. Cell-to-cell whispers at the entrance to the brain and gut.

August

Sir Paul Nurse (PhD), Nobel Laureate, President Rockefeller University, New York, United States of America. Cell cycle control.

Dr Andrea McNeill, Malaghan Institute of Medical Research. EAE, modified superantigens and regulatory T cells.

Dr Peter Martin, Respiratory Physician, Wakefield Specialist Medical Centre, Wellington, New Zealand. TB: yesterday, today and tomorrow.

Prof Carolyn Geczy, Head Inflammatory Diseases Research Unit, University of New South Wales, Australia. New ways of regulating processes in inflammation.

September

Kylie Quinn, Malaghan Institute of Medical Research. T regulatory cells and their impact on mycobacterial infection or vaccination.

Dr David Ackerley, School of Biological Sciences, Victoria University of Wellington, New Zealand. From bioremediation to anti-cancer gene therapy: directed evolution of bacterial oxidoreductases.

Assoc Prof Ian van Driel, Molecular Science and Biotechnology Institute, University of Melbourne, Australia. Protection from gastric autoimmune disease requires extrathymic T cell deletion and immune suppression.

Dr Shiva Reddy, School of Biological Sciences and Department of Paediatrics, University of Auckland, New Zealand. Early beta cell damage as a trigger for type I diabetes.

Dr Jilly Evans, VP, Biology Amira Pharmaceuticals Inc, San Diego, United States of America. Development of anti-inflammatory therapies in the leukotriene pathway.

October

Marina Harvie, Malaghan Institute of Medical Research. A tantalising tale of Th2 immunity…

Dr Nicola Dalbeth, Department of Medicine, University of Auckland, New Zealand. Mechanisms of bone erosion in chronic gout.

November

Rachel Perret, Malaghan Institute of Medical Research. Generation of tumour-protective memory T cells.

Lisa Goldsack, Malaghan Institute of Medical Research. CD4+ T cell memory and IFN-γ.

Dr Troels Petersen, Malaghan Institute of Medical Research. PAMP cocktails, dendritic cell maturation and tumour protection.

December

Clare Bai, Malaghan Institute of Medical Research. The role of T regulatory cells in Multiple Sclerosis.

Janet Siebert, CytoAnalysis, United States of America. Techniques for coping with complex multi-dimensional data sets generated by flow cytometry.

Education

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

Doctoral Candidates

In 2006, the Malaghan Institute supported the following PhD students by assigning them to a senior scientist to guide and advise their work. Their studies not only help them satisfy their thesis requirements but also contribute to the core research programmes of the Institute.

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

Clare Bai *(BSc, MSc(Hons))* "The role of T regulatory cells in autoimmunity"

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

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

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

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

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

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

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

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

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

Nicholas van Panhuys *(BSc(Hons))* "Basic biology of the Th2 immune responses in protective immunity and allergic diseases"

Catherine Weir *(BSc(Hons))* "T cell modulation in EAE"

The following students had their theses accepted and were awarded their Doctorates in 2006:

Patries Herst *(BSc, MSc, MPhil)* "Trans-plasma membrane electron transport: physiological importance in the ρ^0 model of aerobic glycolysis"

Victoria Watt *(BTech(Hons))* "Regulatory mechanisms of graft versus host disease"

Masters Students

In 2006 the Malaghan Institute hosted two students from Göteborg University, Sweden. The research the students undertook during their time at the Institute will contribute towards their Masters degrees.

Jeanette Söederbom *(BPharm)* "Inhibition of immune responses by modified superantigen"

Therése Pettersson *(BPharm)* "Development of a novel DNA plasmid replicon vaccine for *Mycobacterium tuberculosis*"

Honours Student

In continuing our relationship with Victoria University the Malaghan Institute hosted an Honours student in 2006. The research project was tendered out by the Institute and undertaken by the following successful applicant as a contribution to his Honours study.

Sam Gusscott *(BBmedSc)* "Proteomic profile changes during dendritic cell maturation"

Summer Student

Each year, the Malaghan Institute hosts summer interns who have an interest in science, and are of the calibre to take on and benefit from an assigned research project at the Institute. Working with close direction from the Institute staff, they are able to conduct meaningful work and learn what a career in research offers. In 2006/07, we fostered the following student:

Sophie Robinson *(MBChB, 4th year)* "Identification of respiratory pathogens in nasopharyngeal aspirate (NPA) samples from infants hospitalised with Bronchiolitis (2003-2005)"

Community Education

At the Malaghan Institute, we are dedicated to disseminating the knowledge gained through our research to the community. In 2006, we had 16 community groups tour the Institute. The groups had the opportunity to meet the Malaghan's internationally acclaimed scientists, learn about the immune system and experience medical research in action. In addition our staff gave presentations to nine clubs, community groups and schools offsite.

Operations Report

Over the past year the Malaghan Institute Operations have really started to run smoothly. At the same time last year we were struggling to maintain basic necessities, such as climate control. We had a spate of building alarms, mostly handled by senior staff, and costly service calls. Most of our operation time was spent resolving issues associated with the building and faults not apparent when the building was commissioned.

However, in 2006 we progressively took control with a better understanding of the building plant and facilities. Stabilising the existing services has allowed us to add our own unique engineered solutions, fine-tuning the facility to meet our own exact requirements.

As part of this fine-tuning we commissioned an Energy Use audit from Setpoint Solutions Ltd, in order to evaluate our energy consumption and energy management practices. This report provided some excellent analysis of our setup as well as many recommendations for improving efficiency, an area of increasing global concern recently. We would like to gratefully acknowledge the work of Setpoint Solutions Ltd, who offered their services free of charge in support of the work done at the Institute.

A key project this year was to provide an extract system for the BD FACSVantage DiVa FACS sorter that protects the operator from harm while working with potentially hazardous samples. The project, sponsored by AMI, was a collaboration between Thermoplastics Ltd, the VUW workshop and Malaghan Institute Flow Cytometry Suite Manager Kylie Price. We are delighted with the results of the project as many of the cancer tissue samples are potentially very dangerous and this extract allows us to get full use from our most important analytical device while ensuring the safety of our staff.

This year also saw the completion of two major construction projects: the reception wind lobby and the new animal housing room. Although managed by Victoria University, both projects required a lot of input from our own senior staff, from the original design specifications through some rigorous testing and fault-finding, to successful completion.

The IT infrastructure of the Institute also received a significant overhaul this year. We run a cross-platform network of both Macintosh and Windows-based machines. Traditionally Macs have been perceived as being behind in terms of networking but in the last couple of years have made great strides in improving performance in this area. As most of our research staff work on Macs, we invested in a Macintosh server, which allows us to centralise and secure many functions, particularly data storage. To accommodate the increase in network usage, we also updated our network hardware to allow faster access to the new server. As a result, our researchers now have access to a cutting-edge environment for cross-platform network services.

The goals for the Operations Team in the coming year are focused on improving efficiency, both through the uptake of the recommendations of the Energy Audit and through updating the systems needed for good management of the facility. As our numbers, both of staff and floor space, continue to increase there is more strain placed upon our day-to-day operations and the challenge for us is to continue ensuring that we provide the best resources for our researchers and a facility in which good, robust science can be performed.

Laurence Fallon, Dominique Hawinkels, Darrell Smith and Mike Zablocki
THE OPERATIONS TEAM

Fundraising Report

Malaghan Institute of Medical Research

I really need to begin my report by thanking all those who contributed to a very successful fundraising year: the Malaghan Institute Friends Committees, our faithful volunteers, our many sponsors, the various granting authorities who believe in our research and the public of New Zealand who generously gave so much.

The Friends of the Malaghan Institute have once again proven to be top supporters by organising several stunning events in Wellington, Hawkes Bay and Auckland. The Friends groups are made up of fantastic and passionate volunteers who quietly toil behind the scenes to put on several fabulous events throughout the year, which raise significant money for the research projects at the Malaghan Institute. In addition to the annual Lollipop Appeal and the regional Golf Tournaments, the following events were also held throughout the country: a Rock and Roll Night and Doctors and Nurses Bash in Auckland, a Wine and Olive Oil Presentation hosted by Sileni Estates and the Village Press, a Ladies Luncheon in the Hawkes Bay, and a cocktail party in Queenstown. We were also lucky to have benefited from ArtWorks, held late in the year at the Hilton Hotel in Auckland. So I would like to say a huge thanks to all the Friends of the Malaghan Institute for all their hard work throughout the year and for the superb events they hosted.

A lot of the work that goes on at the Malaghan Institute would simply not be possible without the support of our loyal Sponsors and Benefactors, and the organisations that provide us with grants. Therefore, a special and heartfelt thanks must go to all our supporters and funding sources (see following pages). I would like to make a special mention of AMI, who were not only principal sponsors of our Lollipop Appeal, but who also supported several other events throughout the year, such as the regional Golf Tournaments. So thank you AMI – I look forward to working with you again in 2007.

The work of the Fundraising Team also includes liaison and interaction with many community groups. As part of this work we were pleased to host 16 community groups for tours of the Malaghan facilities and we had Scientists go out and present our research to nine clubs, schools and groups off-site. Throughout the year representatives from the

Institute also visited the Retirement Villages of Ryman Healthcare, presenting our research to their residents in appreciation of a year of their fundraising.

2006 brought with it many changes to the Fundraising Team. We were very sad to see Manager Rochelle Stevens leave in May after four years of passionate support for the Institute's work. I enthusiastically stepped into the Managers role and in December, Tanya Shennan was appointed Community Liaison for Fundraising – a newly created position with a focus on community interaction. In May, Dr Debbie Scarlett joined the Fundraising team as a part-time Communications Assistant. Debbie worked previously as a Post-doctoral Research Fellow in the Asthma and Cancer Cell & Molecular Biology groups and her research background has enabled us to expand our profile through the preparation of communication projects for both the public and scientific arenas. We also enjoyed the pleasure of Amy Millward's communication expertise for three months from May to July and are grateful to Neil Fisher for his assistance with various projects throughout the year.

We look forward to 2007 and the opportunity to support the many worthwhile medical research programmes at the Malaghan Institute.

With many thanks to all those who support us,

Anthea Armstrong
FUNDRAISING AND COMMUNICATIONS MANAGER

Wellington Friends

Robyn Vavasour (Chair)
Judy Blair
Adrienne Bushell
Penny Catley
Gaye Carroll
Annemarie Janssen
Jill Kinloch
Susan Laurenson
Jill Strang
Maureen Cameron

Wellington Fundraising Functions 2006:

Lollipop Appeal
ING NZ Ltd Malaghan Golf Tournament

Hawkes Bay Friends

David Mossman (Chair)
Bry Mossman
Denise Bull
Margie Dick
Beth Kay
Angela Miller
Andy Neilson
Jan Patterson
Bruce Speedy
Lynn Spence
John Stovell
Terry Thornton

Hawkes Bay Fundraising Functions 2006:

Malaghan Golf Tournament
Ladies Luncheon

Auckland Friends

Neil Malaghan (Chair) (to Mar)
Judy Jordan (Chair) (from Mar)
Mary Collow
Steve Culpan (from Oct)
MaryAnne Ellett (from Oct)
Nicholas Glanfield
Elaine Haggitt
Margaret Malaghan
Raewyn Roberts

Auckland Fundraising Functions 2006:

AMI Insurance Malaghan
Golf Tournament
Rock n Roll Evening
Doctors and Nurses Bash

How You Can Help

Malaghan Institute of Medical Research

How Can You Help Us Lick Cancer, Asthma, Arthritis, MS and Infectious Disease?

The Malaghan Institute is independent and receives no direct government funding. It is reliant on contestable research grants and contributions from corporate sponsors, trusts, bequests, individuals and fundraising initiatives.

The Malaghan Institute is at the forefront of international medical research. We have the most committed and qualified team of scientists working around the clock on the toughest, and most urgent, human diseases. We are making good progress toward the ultimate goal of developing effective treatments and vaccines for some of the world's most dangerous and debilitating diseases, but without funding the work will stop and the 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 medical research at the Malaghan Institute of Medical Research.

Corporate Sponsorship

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

Donations

Donations from individuals and Trusts form a large part of our funding. Income is used to support the research programmes and are acknowledged by a personal letter and receipt.

All donations over $5 are tax-deductible.

Bequests

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

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

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

· A percentage (%) of my estate or

· The following property and assets or

· The residue of my estate or

· The amount of $ (in words) or

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

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

Should you require any additional information about the above options or have any queries, please contact:
The Development and Communications Manager
Malaghan Institute of Medical Research, PO Box 7060, Wellington, New Zealand
+64 4 499 6914

Please browse our website – *www.malaghan.org.nz*

Funding Sources

Malaghan Institute of Medical Research

Grants, Trusts and Foundations

A H Malaghan Trust
AMI Insurance
Arthur N Button Charitable Trust
Austrian Science Fund (FWF)
Centocor
Foundation for Research, Science & Technology
Genesis Oncology Trust
Harry and Beverley Romanes
H B Williams Turanga Trust
Lion Foundation
LL & ZL Meller Charitable Trust
Marjorie Barclay Trust
Merck, Sharp & Dohme, NZ
Milne Trust
Morris Cancer Research Foundation Trust
Neurological Foundation
New Zealand Cancer Society
New Zealand Cancer Society – Wellington Division
Novogen Inc
Peter C SE Leuchars Family Trust
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Wellington Medical Research Foundation

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Duxton Hotel
East Coast Forklifts Ltd
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Faith Taylor
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First NZ Capital
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Golf Imports Ltd
Grove Restaurant
Harry Romanes
Hawkes Bay Painting
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Jeremy Corbett
John Balmforth
John Croskery Golf Today NZ Ltd
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K and J O'Connor
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Kit Jackson
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Lion Nathan Ltd
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McKay Shipping Ltd
Malcolm Small
Mana Coach Services Ltd
Mangawhero Farm
Manukau Golf Club
Margaret Neave Trust
Martin Bosley's Yacht Club Restaurant
Matthew Malaghan
Maxwell's Golf Retreat
Mazda Motors NZ Ltd
MIA Trust
Mudgeway Partsworld
Muritai Lodge
Murray Higgins
Museum Hotel
National Bank of New Zealand
Nestle NZ Ltd
Nicola Harvey
Nice & Natural Ltd
Norsewear Ltd
NOW Couriers
NZ Bi Products Ltd
Oceanbridge Shipping Ltd
OM Financial
Onesource Group Ltd
Opus International Consultants Ltd
Orton Catering Ltd
Pak Line Ltd
Paris House
Parker and Associates
Pearson Investment Advisory Ltd
Peter Shirtcliffe
Porter Hire Ltd
Pravda Restaurant
Rainbow Print
Rebecca L Roberts
Red Current
Regency Duty Free Ltd
Regional Health
Renaissance Ltd
Resene Paints Ltd
Robin Hill
Roger Butland
Rotary Club of Queenstown
Rotary Club of Upper Hutt
Rutherford & Bond Toyota
Ryman Healthcare Ltd
S Iorns
Saunders Unsworth
Senate Communications
Signwise Auckland Ltd
Sileni Estates
Smith & Smith
Spice Island Restaurant
Spy Valley Wines
S Russell
Stevenson
Stockco Ltd
Stone Pine Lavender
Taylor Preston Ltd
Tetley-Jones Thom Sexton
The Beluza Co Ltd
The Cut Magazine
The Royal Wellington Golf Club
The Wellington Company
The White House Restaurant
Tip Top Ice-Cream Ltd
Tony Robinson
Turners & Growers Ltd
Tussock Grove Boutique Hotel
Upper Hutt 60's Up Movement
Urban Retreat
Urban Sanctuary
Vavasour Wines
Vista Restaurant
Wairakei International Golf Course
Wairakei Resort Hotel
Wairoa Veterinary Services Ltd
Waterford Security Ltd
Wellington Rugby Football Union
Wellington Star – Mercedes-Benz in Wellington
Wendy Jones Pinkettes
West Plaza & Bay Plaza Hotels
Whakatu Coldstores Ltd
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Bequests

Susan L Amon
Tui Armstrong
Irene Brisco
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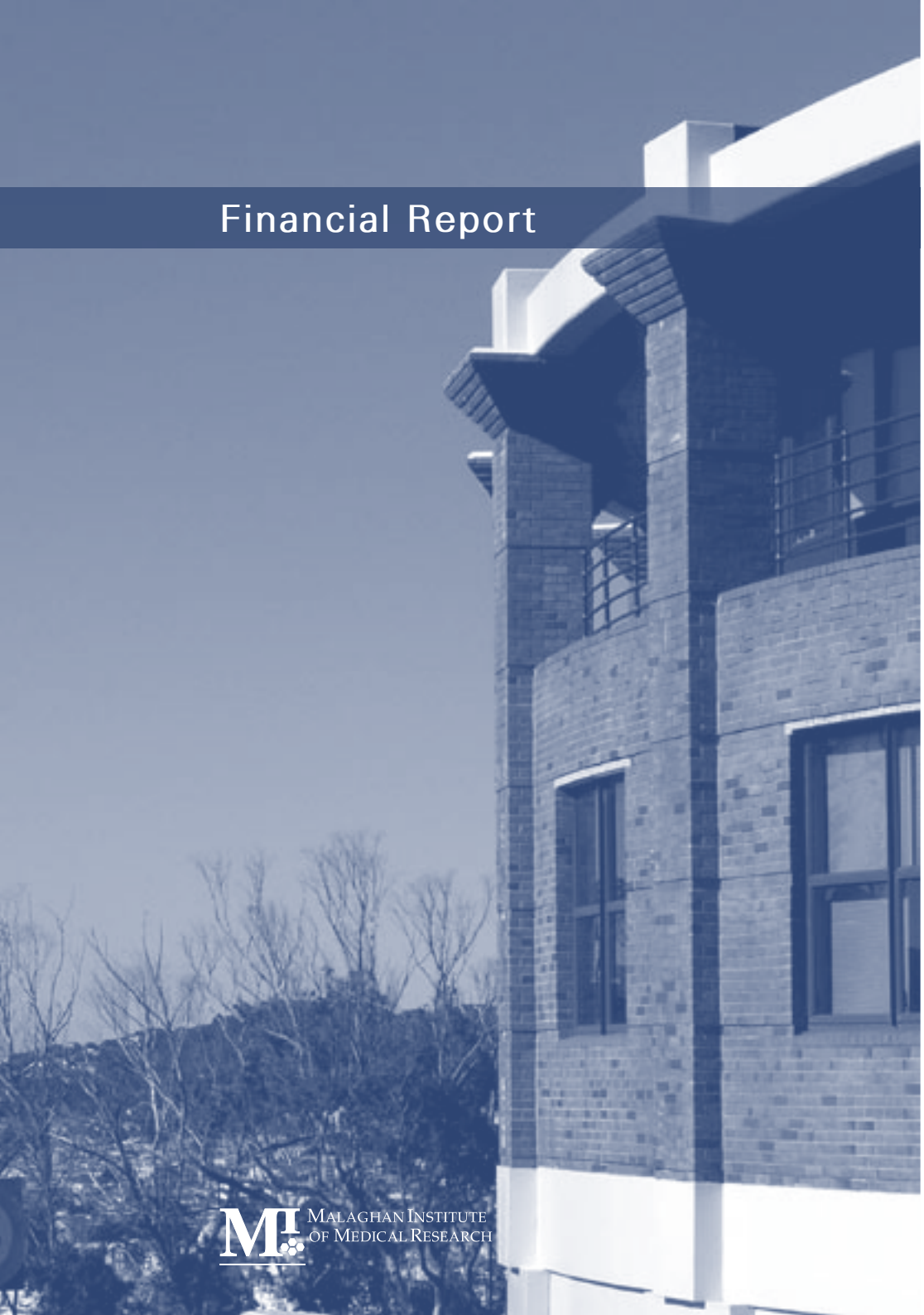
B B Stoker
Susan May Thompson



Financial Report

The Institute has continued to grow in 2006 and has faced many new challenges. As our staff numbers increased we have extended our floor space and operating costs. These increased costs have fortunately been offset by our scientists' recent successes in obtaining fully costed grants. In particular, our Health Research Council programme grant was reviewed and renewed. This grant supports three senior scientists and ensures their tenure for the next three years.

We have been fortunate to have successfully obtained funding for nearly $450k worth of new equipment and science infrastructure. As always, without this additional support, we would not be able to continue operating as we do not generate sufficient funds to cover our depreciation expense.

Our thoughts and thanks go to our loyal supporters who not only support us regularly over the years but have remembered us in their wills and left a bequest to our Capital Endowment Fund. Returns from this Fund have continued to provide much needed support for the science activities of the Malaghan Institute. We have continued to grow this Fund thanks to the prudent guidance of David Wale who generously gave us support in this area. Furthermore, the high interest rates which have been a feature of the 2006 year have provided good returns on our term deposits, which have been invested in science and operational activities.

The Finance Team look forward to continuing to provide a sound and efficient financial platform which will support the challenging scientific activities of the Malaghan Institute.

Susie Whelan and Janine Gray
FINANCE TEAM

Malaghan Institute of Medical Research

Auditors Report

Deloitte.

TO THE TRUSTEES OF THE MALAGHAN INSTITUTE OF MEDICAL RESEARCH INC

We have audited the attached summary financial statements of the Malaghan Institute of Medical Research (the "Institute") for the year ended 31 December 2006.

Trustees' Responsibilities

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

Auditors' Responsibilities

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

Basis of Opinion

We conducted our audit in accordance with New Zealand Auditing Standards. We planned and performed procedures to ensure the summary financial statements are consistent with the full financial statements on which the summary report is based. We also evaluated the overall adequacy of the presentation of information in the summary financial statements against the requirements of FRS-39: *Summary Financial Reports*.

Other than in our capacity as auditor, we have no relationship with or interests in the Institute.

Opinion on the Summary Financial Statements

In our opinion, the amounts set out in the summary consolidated financial statements for the year ended 31 December 2006 have been correctly taken from the full audited consolidated financial statements of the Institute from which they were extracted.

In common with organisations of a similar nature, control over the revenues from donations 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's full audited financial statements contained a qualified audit opinion.

For a better understanding of the scope of our audit for the Institute's consolidated financial statements and of the Institute's financial position, financial performance and cash flows for the year ended 31 December 2006, this report should be read in conjunction with the Institute's audited consolidated financial statements for that period.

Our examination of the summary consolidated financial statements was completed on 15 March 2007 and our opinion is expressed as at that date.

Chartered Accountants
WELLINGTON, NEW ZEALAND

This audit report relates to the summary financial statements of Malaghan Institute of Medical Research (the "Institute") for the year ended 31 December 2006 included on Malaghan Institute of Medical Research's website. The Board of Trustees is responsible for the maintenance and integrity of the Institute's website. We have not been engaged to report on the integrity of the Institute's website. We accept no responsibility for any changes that may have occurred to the summary financial statements since they were initially presented on the website. The audit report refers only to the summary financial statements named above. It does not provide an opinion on any other information which may have been hyperlinked to/from these summary financial statements. If readers of this report are concerned with the inherent risks arising from electronic data communication they should refer to the published hard copy of the audited summary financial statements and related audit report dated 15 March 2007 to confirm the information included in the audited summary financial statements presented on this website. Legislation in New Zealand governing the preparation and dissemination of financial statements and summary financial statements may differ from legislation in other jurisdictions.

Financial Accounts

Malaghan Institute of Medical Research - Abridged Accounts 2006

Consolidated Statement of Financial Performance For year ended 31 December	2006 Consolidated	2005 Consolidated
Income - Operating		
Income from Donations	503,420	657,057
Income from Scientific Grants	3,748,813	3,256,100
Interest and Income from Investments	178,124	142,299
	4,430,357	4,055,456
Expenses - Operating		
Salaries	2,319,049	2,146,234
Expenses (including depreciation)	2,933,826	2,618,308
	5,252,875	4,764,542
Operating (Deficit)	**(822,518)**	**(709,086)**
Plus Grant Income for Fixed Asset Purchases	438,934	195,171
Transfer from Capital Endowment Fund	262,114	229,828
Transfer (to)/from Research Reserve	(40,000)	15,951
Net (Deficit) after capital grants and transfers (to)/from reserves	**(161,470)**	**(268,136)**
Capital Endowment Fund Income		
Investment Income	548,829	432,200
Bequests	260,934	137,976
	809,763	570,176
Transfer to Operating Account	(262,114)	(229,828)
Retained in the Capital Endowment Fund	**547,649**	**340,348**

Consolidated Statement of Movements in Equity For year ended 31 December	2006 Consolidated	2005 Consolidated
General Reserve		
Opening Balance	1,400,512	1,668,648
Transfer of Net (Deficit)	(161,470)	(268,136)
	1,239,042	**1,400,512**
Capital Endowment Fund		
Opening Balance	3,966,711	3,626,363
Income Retained	547,649	340,348
Closing Balance	**4,514,360**	**3,966,711**
Research Reserve		
Opening Balance	56,932	72,883
Transfer to General Reserve	40,000	(15,951)
Closing Balance	**96,932**	**56,932**
Total Funds	**5,850,334**	**5,424,155**

Consolidated Statement of Financial Position As at 31 December	2006 Consolidated	2005 Consolidated
These funds are represented by:		
Current Assets	2,878,402	2,334,706
Less Current Liabilities	3,067,656	2,415,667
Plus Fixed Assets	1,525,228	1,538,405
Plus Investments	4,514,360	3,966,711
Total Equity	**5,850,334**	**5,424,155**

Consolidated Statement of Cash Flows For year ended 31 December	2006 Consolidated	2005 Consolidated
Net Cash Flow from Operating Activities	1,373,063	839,525
Net Cash Flow from Investing Activities	(851,310)	(605,120)
Net Cash Flow from Financing Activities	(2,374)	(5,353)
Net Increase in Cash Held	519,379	229,052
Cash at Beginning of the Year	2,043,138	1,814,086
Cash at End of the Year	**2,562,517**	**2,043,138**

These Summary Statements were authorised for issue by the Trust Board of the Malaghan Institute of Medical Research at a meeting held on 15 March 2007.

Financial information was extracted from the audited Financial Statements of the Malaghan Institute of Medical Research for the year ending 31 December 2006. The summary financial report cannot be expected to provide as complete an understanding as provided by the full financial report of the financial performance, financial position, and cash flows. A full copy of the Financial Statements including Notes can be obtained on request to the Financial Manager, Malaghan Institute of Medical Research, PO Box 7060, Wellington South, New Zealand.

Directory

Malaghan Institute of Medical Research

Board of Trustees

Mr John Beattie *LLB(Victoria)*

Prof David Bibby *DSc(Loughborough University)*
Assoc Prof John Carter *BMedSc, MBChB(Otago), FRACP, FRCPA*

Mr Bryan Johnson *BCA(Victoria)*

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

Mr Graham Malaghan *FCILT (Chairman)*

Dr David Mossman *BVSc, MRCVS, MNZIF*

Prof John Nacey *MBChB, MBA, MD(Otago), FRACS*

Mr Gary Quirke *BCA, CA, FCILT*

Dr Jim Watson *PhD(Auck)*

Mr C Dan Williams *CA*

Staff of the Institute 2006

SCIENTIFIC

Director of Research

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

Group Leaders

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

Prof Mike Berridge *BSc, MSc(Hons), PhD(Auck)* - Cancer Society Senior Fellow

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

Dr Ian Hermans *BSc(Hons)(Otago), MSc(Distinc)(Otago), PhD(Victoria)* - Sir Charles Hercus Health Research Fellow

Dr Joanna Kirman *BSc(Hons)(Otago), PhD(Otago)* - Sir Charles Hercus Health Research Fellow

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

Staff Scientists

Stephanie Huck *BSc(Massey) - Manager BRU*

Kylie Price *BSc(Otago), MSc(Hons)(Victoria) - Flow Cytometry Suite Manager* (from Jan)

Joanna Roberts *BMedSci(Otago) - Flow Cytometry Suite Manager* (to Feb) *U*

Julie Walton *BSc(Massey) - Clinical Trials Project Manager*

Visiting Researchers

Dr Anil Ranchord *MBChB(Otago)* (from Dec)

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

Senior Research Fellows

Dr Patrizia Stoitzner *MSc, PhD(Innsbruck)*
Dr Melanie McConnell *BSc, PhD(Otago)* (from Aug)

Research Fellows

Dr James Baty *BSc(Hons), PhD(Otago)* (to Feb)

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

Dr Andrea McNeill *BCA/BSc(Hons)(Victoria), PhD(Otago)* (to Aug)

Dr Troels Petersen *MSc, PhD(Copenhagen)*

Dr Debbie Scarlett *BSc(Hons), PhD(Otago)* (to May)

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

An Tan *BSc(Victoria)*

Senior Research Officers

Kate Andrew *BSc(Hons)(Otago)* (to May)

Mali Camberis *BSc(Victoria)*

Elizabeth Chia *BSc(Burnaby)*

Kathryn Farrand *MSc(Massey)*

Melanie Prout *BSc(Hons)(Victoria)*

Fenella Rich *BSc(Hons)(Otago)*

Dr Jianping Yang *MB(Shanxi Medical University)*

Research Officers

Oliver Chow Worn *BSc(Hons)(Surrey)* (to Nov)

Lisa Goldsack *BBmedSc(Hons)(Victoria)* (to May)

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

Laura Green *BS(Madison)* (from Jun)

Dr Jae Jung *BS(California), MD(Washington), PhD* (to May)

Sara Mirmoeini *BBmedSc(Hons)(Victoria)* (from Aug)

Jim Qin *BSc(Hons)(Auckland)*

Natalie Redshaw *BSc(Hons)(Bradford)*

Evelyn Spittle *MSc(Otago)*

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

Research Nurse

Catherine Wood *RN, BN, PGDipHealSci*

Research Assistants

John Bensemann (to Jan)

Sharon Brokenshire (from May)

Charlotte Cheriton (from Apr)

Nicola Kofoed *BSc, DipGrad(Otago)* (from Jul)

Kelly Locke (from May)

Katherine MacGregor *BSc(Massey)* (from Nov)

Rene McLaughlin *BBmedSc(Victoria) (P/T)* (from Jul)

Amy Millward *BSc, BA(Massey)* (to May)

Jennifer Ogle *BSc(Massey)* (to Aug)

Fiona Park *DipAg* (to Sep)

Anna Robertson (to Mar)

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

PhD Students

Haley Ataera *BSc, MSc(Victoria)* (from Jan)

Clare Bai *BSc, MSc(Hons)(Auckland)* (from Jan)

Nina Dickgreber *DipSci(Kiel)* (from Jun)

Lisa Goldsack *BBmedSc(Hons)(Victoria)* (from May)

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

Marina Harvie *BSc(Hons)(Victoria)*

Patries Herst *BSc, MSc(Netherlands), MPhil(Waikato), (P/T)* (to May)

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

Rachel Perret *BSc(Hons)(Otago)*

Kylie Quinn *BSc(Hons)(Otago*)

Dianne Sika-Paotonu *BSc, BBmedSc(Victoria)* (from Jul)

Helen Simkins *BSc(Hons)(Otago)*

Nicholas van Panhuys *BSc(Hons)(Victoria)*

Victoria Watt *BTech(Hons)(Auckland)* (to Dec)

Catherine Weir *BSc(Otago), (Hons)(Victoria)*

Masters Students

Jeanette Söederbom *BPharm(Göteborg*)

Therése Pettersson *BPharm(Göteborg)*

Honours Student

Sam Gusscott *BBmedSc(Victoria)*

Summer Student 2006/2007

Sophie Robinson *MBChB(Otago)* (4th year)

Research Consultants

Assoc Prof John Carter, Wellington Cancer Centre

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

Prof Brett Delahunt, University of Otago

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

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

Dr Anne La Flamme, Victoria University

Dr David Ritchie, Peter MacCullum Institute, Australia

SCIENCE SUPPORT AND ADMINISTRATION

Administration

Carolyn Hallsmith -*Receptionist (P/T)* (from Oct)

Finance

Susie Whelan *CA, NZIMDip - Finance Manager*

Janine Gray *BCA(Victoria) - Senior Accounts Clerk (P/T)*

Fundraising

Anthea Armstrong *BBS(Massey) - Fundraising & Communications Manager*

Neil Fisher BSc, *GDipBmedSc - Fundraising Assistant (P/T)* (Feb to Nov)

Amy Millward *BSc, BA(Massey) - Fundraising Assistant* (May to Jul)

Dr Debbie Scarlett *BSc(Hons), PhD(Otago) - Communications Assistant (P/T)* (from May)

Tanya Shennan *BSc(Victoria) - Community Liaison Officer* (from Dec)

Rochelle Stevens *BA(Victoria) - Development & Communications Manager* (to May)

Operations

Laurence Fallon - *Lab Assistant/General Admin*

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

Darrell Smith *MSc(Hons)(Victoria), (Dip A.T.)(Wgtn Poly), BSA(Massey) - Facilities Manager*

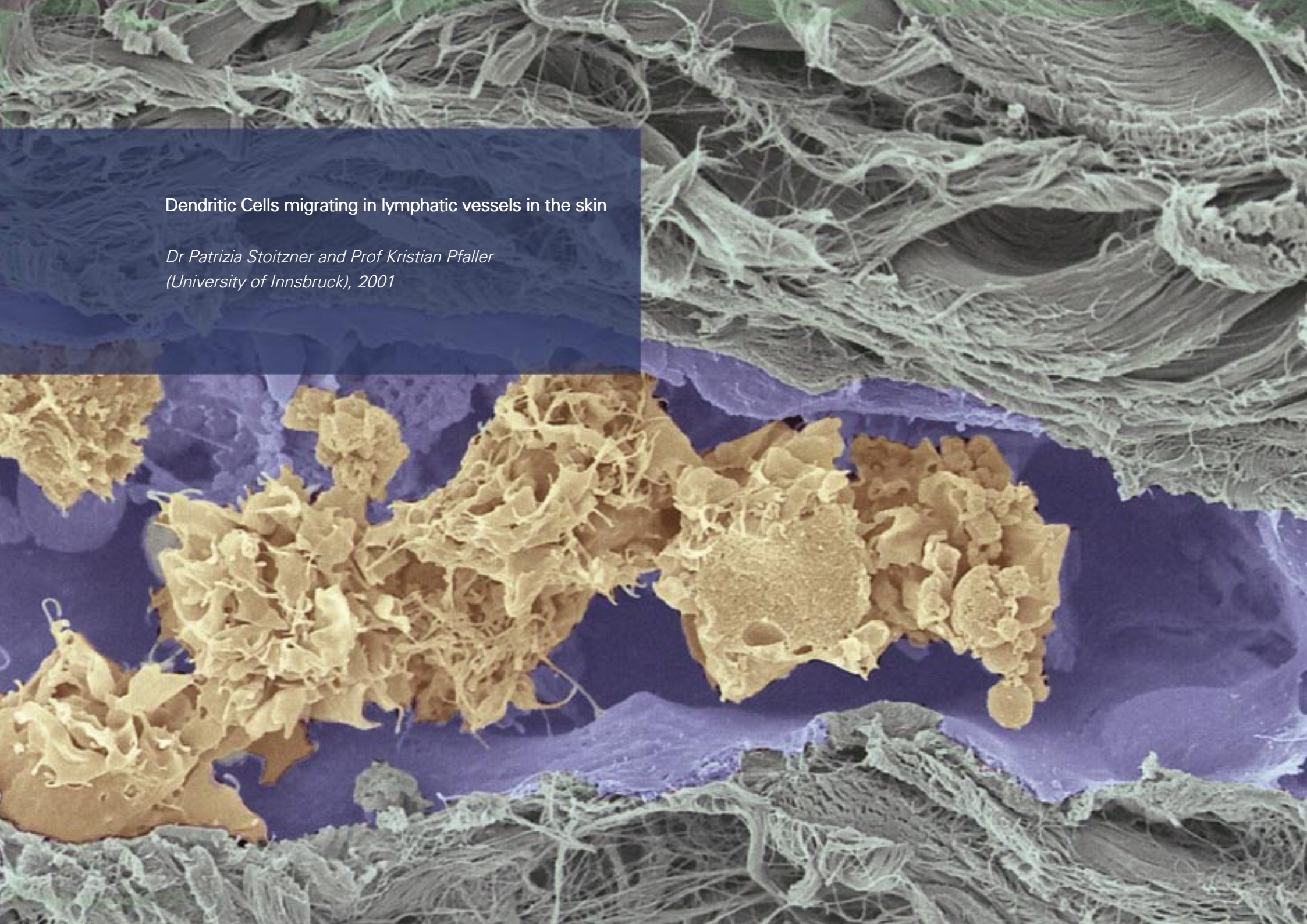
Michal Zablocki *BA(Hons)(Bristol) - Operations/IT Manager*

PA to Director (Human Resources)

Gabrielle Dennis *RSA(English), Pitmans*

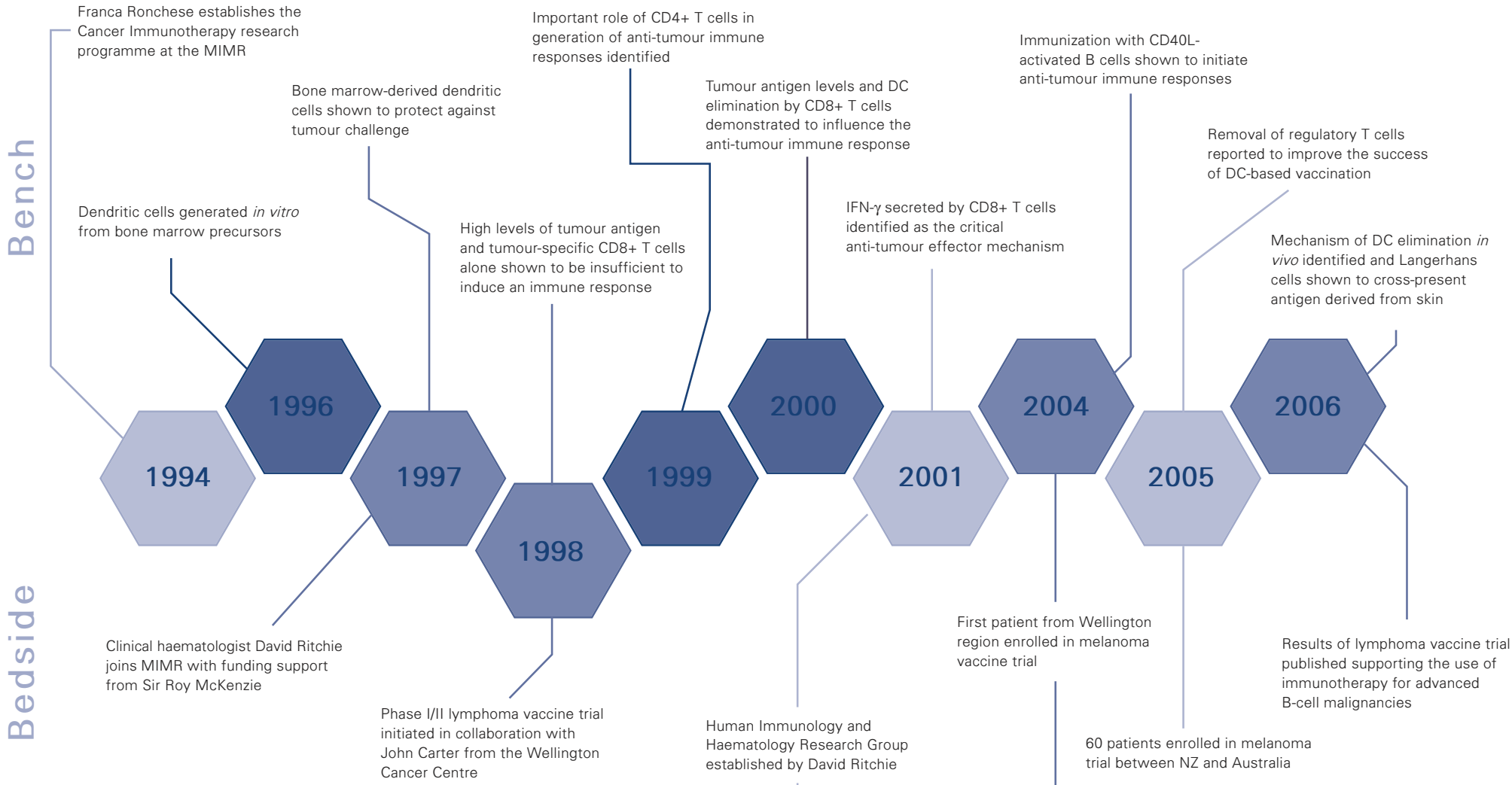
Advisors

Auditors
Deloitte
Bankers
The National Bank
Investments
David Wale
Solicitors
Simpson Grierson



Dendritic Cells migrating in lymphatic vessels in the skin

Dr Patrizia Stoitzner and Prof Kristian Pfaller (University of Innsbruck), 2001



From Bench to Bedside: A timeline of the key research discoveries and clinical developments in the Malaghan Institute of Medical Research Cancer Immunotherapy and Vaccine Research programmes

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