



Annual Report

2017



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Front Cover: *Trapped in a Swarm:* Hookworm larvae (green) are trapped in the lung by myeloid cells (red), which seem to swarm around the worms like wasps, impeding their migration out to the airways. **Image credit:** Dr. Kara Filbey



About us

The Malaghan Institute is New Zealand's leading independent biomedical research institute. For more than 50 years we've been delivering cutting-edge medical research, advancing our understanding of the underlying causes of disease with the goal of finding new options for treatments and cures.

We believe that the key to prevention, treatment and ultimately finding cures for many illnesses and diseases lies in understanding and harnessing the power of the immune system. By using our body's own defences in the fight against disease, we can find a way to make a positive impact in people's lives.

Our internationally-recognised research programmes are driven by a talented team of New Zealand's brightest and most creative scientists, doctoral students and post-doctoral fellows.

As a registered charity, we rely on the generosity of trusts, bequests and donations as well as contestable grants and corporate sponsorships in order to ensure we can keep delivering high-quality research of global significance. All funding is vital to our continued success and helps us achieve our goals of finding and making available cures for the diseases that affect us most in the 21st century.

**RESEARCH IS OUR JOURNEY,
CURE IS OUR DESTINATION.**

Chairman's Report



Our scientific endeavours, depth of research and clarity of vision have seen the Institute make significant progress in both our short and long-term goals this year.

After seeking a senior programme leader to join the team in late 2016 – a position we were not able to fill – we took the opportunity to revisit our current Strategic Plan. Due for review in 2018, we decided to look out five and 10 years from now as to what we would hope to achieve. This has inevitably resulted in a body of work taking place during 2017, with the intention of the Board being in a position to adopt this vision and updated plan in 2018.

Strategic planning is challenging, both to our senior management team and scientific programme leaders, but also for the Board. Having clarity and identifiable goals will ensure we can continue to have confidence in our journey of delivering research outcomes that benefit our community.

Our major source of contestable grant funding continues to be the Health Research Council of New Zealand, the country's prime source of health science funding. During the year the Ministers of Health and Science and Innovation issued a vision for the HRC's Strategy in Health Research – this was the first combined policy initiative. It gives clarity to the Ministries and the HRC as to what is being sought from the public investment in health research. We welcomed this development and will work to see it being successful.

Philanthropy continues to be a significant component of our current and long-term funding and security. This year saw some significant bequests, with special mention to Mrs Holder, whose combined equity and bond investments saw us receive some \$4m, with an emphasis on our cancer research activities.

The Director and his teams have been kept busy not only with the aforementioned activities, but also some significant progress in our research activities and the capturing of intellectual property developed in the

Institute into two separate commercial entities. These have both senior management and Trustee representation on their Boards.

During the year four golf tournaments and several Science Updates were held in various centres around the country. We are about to embark on another round, both providing good platforms for us to promote awareness of the Institute.

Sadly, this year we lost two important contributors to the Institute: Professor Bill Paul at the National Institutes of Health in Washington DC and Professor Jim Watson, a former member of our Trust Board. Our appreciation for their support and our condolences have been made to their respective families.

Finally, a message of appreciation to my fellow Trustees, management and to all our supporters. It is your efforts that have resulted in a special resource for our country, something to cherish and to benefit all our citizens.

A handwritten signature in black ink, reading 'G. Malaghan'.

Mr Graham Malaghan
ONZM Hon DSc FCILT

CHAIRMAN

Director's Report



In the wake of every exciting new development comes a time for reflection. The Malaghan Institute of Medical Research has been through a fantastic period of growth and scientific achievement. This has resulted in the need to evaluate our capabilities and purpose while still delivering world-class research towards a happier and healthier world.

Our Cancer Immunotherapy programme has progressed into the important stage of bringing its discoveries to patient care, of which the formation of the company Avalia Immunotherapies plays a crucial role in balancing the needs of intellectual property with the needs of fundamental research. We're also moving forward with a programme to develop new forms of cutting edge CAR-T cell technology with our collaborators at Wellington Zhaotai Therapies.

Last financial year Dr Elizabeth Forbes-Blom launched an exciting new platform, supported by both the Government and the National Science Challenges, looking at high value nutrition and how the microbiome in our guts impacts our immunity to infectious agents.

While Dr Forbes-Blom has since taken up an exciting role in Switzerland at Nestlé Research Centre, our commitment to this programme has not changed. The programme has been nuanced into what is now called the Translational Immunology programme, led by the capable and talented Dr Olivier Gasser, an existing star within our ranks.

This Translational Immunology programme builds on the work already established by Dr Forbes-Blom, but now with a focus looking at the immune system in a way that will support and connect not only the allergy programme, the cancer programme and high value nutrition programme – but potentially new areas in the immune system frontier as well.

Our Immune Cell Biology programme is starting to bring real benefit to the allergy programme through its bioinformatics research, harnessing data to gain both big-picture and fundamental understanding of complicated biological processes – providing a platform to reassess and re-evaluate targets for research.

As mentioned by our Chairman, part of this last year has been spent on reflection, asking ourselves the essential question: are we best fit for purpose, can we do things better, how far should we go? Opportunity is huge, and we want to ensure that New Zealand patients do not miss out on anything through lack of insight and forward planning on our part.

I am very motivated by the deepening strength and quality of our research activities across all our disease and fundamental research programmes. This has been brought about by the 'coming together' of donors and the alignment of international collaborations that we have with each research programme area. The Institute is poised to go to a higher level of scientific achievement, and through this continued support we are well set to contribute much more to the health of New Zealanders.

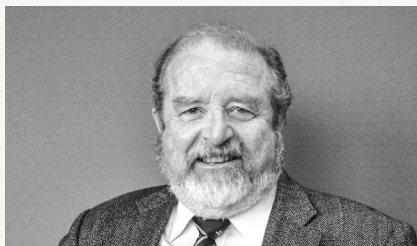
As always, I would like to acknowledge and thank everyone who has supported the Malaghan Institute since 1966, including the Ferrier Institute, the Cawthron Institute and the long-term support from the HRC as well as the backers that allow our fellowships and technological platforms to exist. Our donors, supporters, Friends and advocates play an increasingly important role in helping us achieve our goal in creating a healthy future for New Zealand.

A handwritten signature in black ink, reading 'G. Le Gros'.

Professor Graham Le Gros
CNZM, FRSNZ, FRCPA(Hon)
BSc, Dip Immunol, MPhil, PhD

DIRECTOR

Trust Board Profiles



MR GRAHAM MALAGHAN

ONZM, FCILT, Hon. DSc (VUW) (Chairman)

Appointed Chairman of the Malaghan Institute Trust Board in 1990. Commenced employment at General Foods Corp in 1967, and was appointed General Manager of Refrigerated Freight lines in 1970, acquiring the company in 1987. Was founding Chairman of Tasman Express Line and a member of the LTSA for six years. In 2009 was awarded an Honorary Doctor of Science from Victoria University of Wellington for his key role in rebuilding the Malaghan Institute into the largest independent medical research organisation in New Zealand. Received the Sir Bob Owens award in 2010 for contributions to the transport, logistics industries and the community. Made an Officer of the Order of Merit for his services to medical research and philanthropy in 2012. Current directorships include several private companies.



MS NICOLA SLADDEN

LLB MPH

Appointed to the Malaghan Institute Trust Board in July 2014. Appointed Banking Ombudsman at the Office of the Banking Ombudsman in August 2015 after four and a half years as Deputy Banking Ombudsman. Has at least 15 years' experience in dispute resolution, a law degree from Victoria University and a Masters of Public Health from Boston University. Was previously the Chief Legal Advisor at the Office of the Health and Disability Commissioner and has worked in private practice. Has published and presented on dispute resolution in New Zealand and abroad.



MR JOHN BEATTIE

LLB MAICD (VUW)

Obtained a law degree from Victoria University (1975) and was a Fulbright Scholar to Cornell University (1979). Has been a Trustee of the Malaghan Institute since 1991 and is the Chairman of Malcorp Biodiscoveries Limited, a subsidiary of the Malaghan Institute. Chairman of CropLogic Ltd, Chairman of Fluent Scientific Ltd and Director of Wellington Zhaotai Therapies Ltd. He is also Chairman the NZ Sports Hall of Fame.

He is a Trustee of the Wanaka Festival of Colour, trustee of the NZ Diabetes Foundation, has been a partner in national law firm Kensington Swan, General Manager of Brierley Investments Limited and was the co-founder of Genesis Research & Development Limited with the late Professor Jim Watson, a former Trustee of the Malaghan Institute.



MR MATTHEW MALAGHAN

BCom MBA

Appointed to the Malaghan Institute Trust Board in August 2008. Graduated from Otago University in 1994 with a Commerce degree. Subsequent employment with Refrigerated Freight Lines in Auckland and Melbourne, and Sea Containers Group in London, Madrid and Buenos Aires. Managing Director of the AUSPERL Group with quarrying, processing, sales and engineering operations in Australia, New Zealand. President of the Perlite Institute (USA). Member of the NZ Institute of Directors.



PROFESSOR GRAHAM LE GROS

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

Appointed to the Malaghan Institute Trust Board in 1995. Was awarded a Fogarty Fellowship at the NIH, Washington DC in 1987-1989, then took a scientist position with Ciba-Geigy in Basel Switzerland for five years before returning to New Zealand to take up the appointment as Research Director of the Malaghan Institute in 1994. Is a Professor of the Department of Biological Sciences, Victoria University of Wellington. A Fellow of the Royal Society of New Zealand, in 2014 he has been made a Companion of the New Zealand Order of Merit (CNZM) for his services to medical research.



DR DIANNE MCCARTHY

CNZM, CRSNZ, PhD, MSc(Hons), BA, BSc

Appointed to the Malaghan Institute Trust Board in 2015. Was Chief Executive of the Royal Society of New Zealand (2007-2014) and has over 20 years experience in various management and governance roles in the tertiary education, science and health sectors. Is a Director of Powerhouse Ventures Ltd, the Cawthron Institute, the NZ Institute of Economic Research, and a member of the governance groups of the Dodd-Walls Centre for Photonic and Quantum Technologies, and two National Science Challenges, Ageing Well and Healthier Lives. Is a Trustee of the Hearing Research Foundation (NZ). Made an Officer of the New Zealand Order of Merit for services to education in 2008, a Companion of the Royal Society of New Zealand for services to science in 2015, and a Companion of the New Zealand Order of Merit for services to science, business and women in 2016.

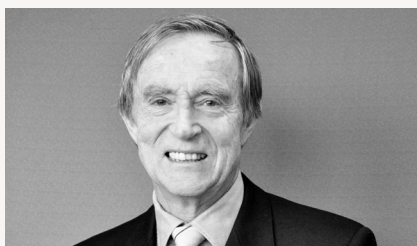


PROFESSOR MIKE WILSON

MA PhD Cantab

Appointed to the Malaghan Institute Trust Board in 2013. Is Pro Vice Chancellor for the Faculties of Science, Engineering, Architecture and Design at the Victoria University of Wellington.

Obtained a 1st class degree in Natural Science from Cambridge University (1980), then obtained a PhD in Physics (1984) after carrying out research with the Radio Astronomy Group at the Cavendish Laboratory. Was appointed as a Lecturer in Applied Mathematics and was subsequently promoted to Senior Lecturer, Reader and Professor of Applied Mathematics (1986) and was appointed as Head of the School of Mathematics at the University of Leeds (2001). In 2005, was appointed as Dean for the Faculty of Mathematics and Physical Sciences at the University of Leeds before joining the Victoria University of Wellington in 2013.



MR BRYAN JOHNSON

ONZM BCA (VUW)

Appointed to the Malaghan Institute Trust Board in 1998. Obtained a commerce degree from Victoria University of Wellington in 1963. Was a senior partner in the stockbroking company Jarden & Co for 25 years and became Chairman after the sale of the business to Credit Suisse First Boston in 1991. Retired from CSFB in December 2000 to further develop his Marlborough winery and vineyard, Spy Valley. Has been a director of various corporations, such as Brierley Investments, Royal Sun Alliance and as Chairman of the Duke of Edinburgh's Award and was a Trustee of the Wellington Stadium Trust. Bryan is also the Founder President of First NZ Capital. In 2015 was made Officer of the New Zealand Order of Merit (ONZM) for his services to business and philanthropy.



DR DAVID MOSSMAN

QSM, BVSc, MRCVS, MNZIF

Appointed to the Malaghan Institute Trust Board in 2005. Attended Lincoln College and then graduated from the University of Queensland in 1965 with a Veterinary Degree. Awarded the Australian College of Veterinary Scientists college prize in 1978 and in 1984 the Coopers NZ Farm Management Award for significant innovative farm management in New Zealand. Keynote speaker at the World Angus and Hereford Conferences. A member of the Lindisfarne College Board 1981-85. Managing Director of private farming, forestry, finance and property companies. President of the Hawkes Bay Friends of the Malaghan Institute and retired rural veterinarian since 2001. Awarded The Queen's Service Medal for services to veterinary science in 2012.



MR IAN PATERSON

QSM, DipAg

Appointed to the Trust Board in 2016 and is Chairman of the Advocacy Group. Ian and his late wife Sally established Just Paterson Real Estate in 1990. Ian donates a considerable amount of his time to charity. He is also an award winning REINZ Auctioneer which proves to be a very useful skill when supporting charities across New Zealand. Awarded Queen's Service Medal for services to philanthropy in 2016..



MR C DAN WILLIAMS

CA

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



PROFESSOR PETER CRAMPTON

MBChB, PhD, FAFPHM, MRNZCGP

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



ASSOCIATE PROFESSOR JOHN CARTER

ONZM, FCILT, Hon. DSc (VUW) (Chairman)

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

Cancer Immunotherapy Programme

The Cancer Immunotherapy programme, led by Professor Ian Hermans, has continued to build on both the melanoma vaccine trial, as well as research combining new generation immunotherapy drugs with vaccine therapies developed at the Malaghan Institute.

Exploring novel ways to produce a sustained immune response to cancers has also required the team to gain a better understanding of innate T cells – profiling them in order to translate preclinical models to clinical trials.

MELANOMA VACCINE

Leading on from the Phase I safety and dosage clinical trial, the Phase II clinical trial is nearing completion. While the Phase II trial has been mechanistic and purely research-driven, the results, which are scheduled to be collated and interpreted in 2018, will provide a great deal of insight for Prof Hermans and his team for future work.

COMBINING T CELL RESPONSE WITH CHECK-POINT INHIBITORS

Immune checkpoint inhibitors such as the drugs Keytruda and Yervoy have emerged in the global marketplace as effective treatments for sustaining an immune response to a tumour.

However, in many cases cancers don't prompt an immune response in the first place – rendering checkpoint inhibitors effectively useless. In response, the Cancer Immunotherapy programme has been looking at the potential of using a cancer vaccine to initiate an immune response in combination with a checkpoint inhibitor to ensure the response is sustained.

"We showed that in our models if we used even just a single shot of checkpoint inhibitor around the time of vaccination, it was enough to keep the T cell response going and even broaden the overall T cell response. By combining the two we were able to completely eradicate tumours 80 per cent of the time in a model of brain cancer," says Prof Hermans.

PROFILING INNATE T CELLS

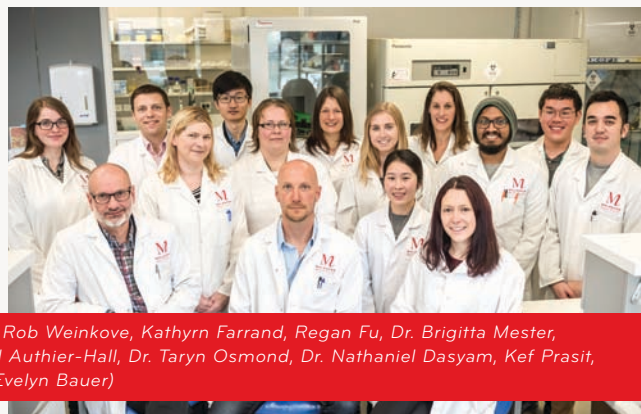
While the unique cancer vaccines developed at the Malaghan Institute hold promise, much more work needs to be done understanding the distinct profile of innate T cells in humans in order to translate the success seen in preclinical models to future clinical work. MBChB/PhD student Ellie-May Jarvis has been undertaking work profiling these innate T cells in cancer patients and their function in the body.

Innate T cell profiling is necessary in order to transition this therapy from animal models to humans, with this work providing a platform for further growth into identifying therapy opportunities for cancers and other diseases.

MAURICE WILKINS CENTRE PROJECT

Another area of research the Cancer Immunotherapy group has been focusing on is to combine immunotherapy with hypoxia-activated chemotherapy, a project funded by the Maurice Wilkins Centre.

Auckland University PhD Student Regan Fu has been based at the Malaghan Institute to investigate whether the naturally oxygen-deprived (or hypoxic) regions within tumours can be used to selectively activate chemotherapy drugs, leaving normal oxygenated tissues unaffected. This may allow immunotherapy and chemotherapy to be used together to increase the overall effectiveness of cancer treatment.



RESEARCH TEAM: (left to right): Ellie-May Jarvis, Prof Ian Hermans, Dr. Rob Weinkove, Kathryn Farrand, Regan Fu, Dr. Brigitta Mester, Dr. Olivier Gasser, Bethany Andrews, Olivia Burn, Ching-Wen Tang, Astrid Authier-Hall, Dr. Taryn Osmond, Dr. Nathaniel Dasyam, Kef Prasit, Joshua Lange (not pictured: Dr. Laura Ferrer-Font, Dr. Giulia Giunti and Evelyn Bauer)

Cancer Cell Biology Programme

In 2016, Professor Mike Berridge and the Cancer Cell Biology programme received the prestigious Liley Medal for an outstanding contribution to health and medical sciences in the field of cell metabolism, for their mitochondrial DNA transfer research published in 2015.

Further collaborative research with Professor Jiri Neuzil and his team of researchers at Griffith University, Gold Coast and the Institute of Biotechnology, Prague, published in the leading online journal *eLIFE*, demonstrated that mitochondrial DNA transfer to tumour cells with damaged mitochondrial DNA involves movement of whole mitochondria, not just the mitochondrial genome.

MITOCHONDRIAL TRANSFER FOLLOWING BONE MARROW TRANSPLANTATION

In Marsden Fund-supported research, the Cancer Cell Biology team is exploring whether mitochondrial transfer from healthy bone marrow donor cells to cells with damaged mitochondria occurs in humans and in a mouse model. Wade Thompson Clinical Research Fellow, Dr Rob Weinkove, has obtained ethical approval to investigate whether mitochondrial transfer from donor to recipient cells occurs in transplant patients to support optimal bone marrow chimera formation.

In a parallel study, PhD student Georgia Carson is using sub-lethal irradiation and bone marrow transplantation to generate mouse bone marrow chimeras to test for signs of mitochondrial DNA transfer in response to damage.

MITOCHONDRIAL TRANSFER DEMONSTRATED IN GLIOBLASTOMA

Another project deleted mitochondrial DNA from cells of an aggressive mouse brain tumour. Cell lines derived from these brain tumours had mitochondrial DNA markers of the mouse into which they were injected and not those of parental tumour cells.

"These cells had recovered their ability to respire and grew as tumours without delay when passaged in mice," says Prof Berridge. "Because neither we nor our collaborators at Griffith University and in Prague have been able to recover glioblastoma cells lacking mitochondrial DNA from frozen

stocks, PhD student Rebecca Dawson is using an alternative method to remove mitochondrial DNA from mouse and human brain tumour cells to overcome this problem."

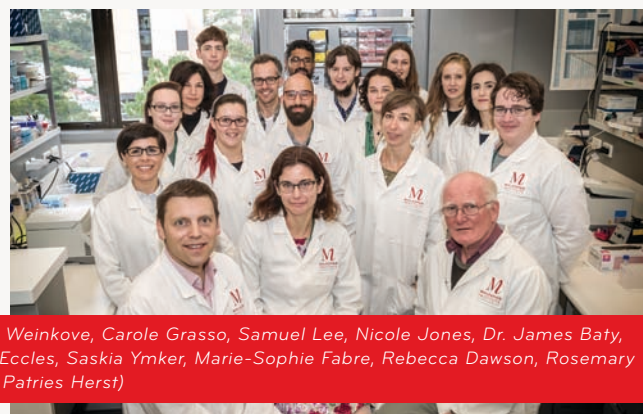
MOLECULAR CONVERSATIONS BETWEEN OUR CELLULAR GENOMES

How mitochondrial and nuclear genomes coordinate their gene expression has remained largely a mystery. A new project aimed at exploring mitochondria-nuclear cross-talk is using breast cancer cell lines frozen in different states of respiration recovery. This novel research could have far-reaching implications for cancer, metabolic diseases like diabetes, cardiovascular diseases and energy-demanding neurodegenerative diseases.

THE ROLE OF BCL6 IN CANCER CELL SURVIVAL

Recently submitted for publication, Dr Melanie McConnell and her team at Victoria University of Wellington have successfully identified a protein found in brain tumour cells - BCL6 – which appears to function as a cell survival mechanism.

Work by Dr McConnell has demonstrated that the BCL6 protein, which is normally found in immune cells, is being expressed in brain tumours that have been exposed to chemotherapy and radiation treatment, potentially contributing to increased survivability of these cancers and diminished response to treatment. Inhibiting this process has also been shown to reverse this effect.



RESEARCH TEAM: (left to right) Leticia Castro, Georgia Carson, Dr. Rob Weinkove, Carole Grasso, Samuel Lee, Nicole Jones, Dr. James Baty, Dr. Melanie McConnell, Remy Schneider, Dinindu Senanayake, Dr. David Eccles, Saskia Ymker, Marie-Sophie Fabre, Rebecca Dawson, Rosemary Gordon, Prof Mike Berridge, Brittany Lewer, Matt Rowe (not pictured: Dr. Patries Herst)

Asthma, Allergy and Parasitic Disease Programme

Understanding how the immune system plays off allergens and infectious agents such as parasites has always been a key area of research at the Malaghan Institute.

Led by Professor Graham Le Gros, the Asthma, Allergy and Parasitic Disease programme looks to better understand the underlying biological processes behind the immune response. Translating that knowledge will lead to better treatments – and in some cases, vaccinations – against diseases like asthma and infections caused by parasites.

HOOKWORM PROGRAMME

The human hookworm parasite is a persistent source of disease and infection. By studying its behaviour using preclinical models, Prof Le Gros and his team have been examining how this parasite interacts with the immune system.

Understanding the fundamental science behind how this worm dampens immune responses that allow it to remain undetected – effectively ‘switching off’ the host’s allergy and autoimmune response – has been a chief focus of research.

In collaboration with the Sabin Vaccine Institute and the Centre for Vaccine Awareness and Research at Texas Children’s Hospital in the United States, the Malaghan Institute has trialled human vaccine candidates in preclinical infection models.

The Sabin Institute’s mission to find new interventions to prevent and treat tropical disease align closely with the Malaghan Institute’s vision for the treatment and cure of diseases.

C.ELEGANS PROGRAMME

Early in 2017, the Malaghan Institute welcomed two visiting researchers from France’s prestigious Centre d’Immunologie de Marseille–Luminy, Dr Nathalie Pujol and Dr Jonathan Ewbank.

Both have brought with them a great wealth of knowledge and expertise around the genetic and cellular processes of

a tiny parasitic nematode worm *C. elegans* which carries many similarities for use in study in humans.

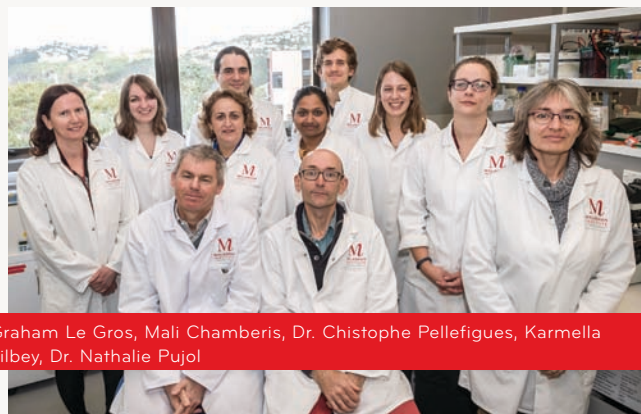
This collaboration merges long-standing experience of nematode genetics and cell biology, providing a new direction for this exciting area of research.

MINION

Dr David Eccles and Dr Ewbank have been sequencing the genome of the parasitic worm *Nippostrongylus brasiliensis* (Np). By sequencing this organism’s DNA, unique insight has been gained of its biology and the genetic mechanisms underlying its mode of infection.

Critical to this development has been the thumb-sized device from Oxford Nanopore Technologies. Called MinION, this technology has allowed Dr Eccles and Dr Ewbank to sequence the Np genome within minutes.

MinION has dramatically increased the speed in which the Malaghan Institute can sequence entire genomes of organisms, generating large amounts of data at a time. Applying this data through bioinformatics allows Prof Le Gros, Prof Franca Ronchese and other researchers at the Malaghan Institute to gain a big-picture understanding of which genes are switched off or turned on when different parasites infect a host organism. Using this knowledge will lead to the Institute gaining a fuller picture of the biological processes surrounding the immune response, helping identify new targets and opportunities for treatments and therapies.



RESEARCH TEAM: (left to right): Melanie Prout, Kimberley Meijlink, Prof Graham Le Gros, Mali Chamberis, Dr. Christophe Pellefigues, Karmella Naidoo, Dr. Jonathan Ewbank, Ferdinand Jagot, Jodie Chandler, Dr. Kara Filbey, Dr. Nathalie Pujol

Immune Cell Biology Programme

Professor Franca Ronchese and her team in the Immune Cell Biology programme have been focused on re-evaluating the relationship between dendritic cells and the immune system.

The use of bioinformatics and transcriptomics to analyse the switching on and off of genes during the immune response has uncovered a number of surprising and unexpected results, which could change the current perspective on what really goes on during an immune reaction.

DENDRITIC CELLS: A FUNDAMENTAL APPROACH

Understanding how dendritic cells initiate and turn off immune responses and educate our immune system has been the primary focus for the Immune Cell Biology team. Much of this relationship remains largely uncharted, so the team has been working to shed light on the fundamental principles behind these interactions.

"Even today, we don't understand the causes of allergic responses, just their symptoms," says Prof Ronchese.

Prof Ronchese's team has been looking at two specific allergens: parasite *Nippostrongylus brasiliensis* and chemical plasticizer dibutyl-phthalate. Studying the responses of Dendritic cells to each allergen using transcriptomics is providing wider insight into which genes are regulated during exposure. Published in the *Journal of Experimental Medicine*, the study found that not only were the two responses vastly different in terms of what genes were transcribed, the presence of type I interferon during the immune response to *N. brasiliensis* was completely unexpected in this type of response.

"This differential regulation of genes and the presence of interferon, something you'd find in a viral infection, was not something we expected to see. We don't think interferon is actually a key mediator, but that it likely exacerbates the allergic response," says Prof Ronchese.

Further work had been done to determine exactly why interferon is there, and what molecules are involved along this unexpected pathway. In the future, Prof Ronchese hopes to continue to look at how dendritic cells interact with other components of the immune system within their environment, and widen this scope to other facets of the immune response.

TRANSCRIPTOMICS

The use of bioinformatics continues to play an integral role in teasing out the relationship between dendritic cells and the immune system. Transcriptomics generates enormous amounts of information. This data undergoes comprehensive statistical analysis using computer algorithms to find biological relationships and trends otherwise invisible by normal investigative means.

The Immune Cell Biology team has recently begun collaborating with the Israeli-based Weizmann Institute in order to look at even bigger sets of data, analysing the transcription response of much larger sets of cells thanks to their advanced technologies and equipment. PhD student Kerry Hilligan spent some time at their facility to exchange techniques and get the collaboration started.



RESEARCH TEAM: (left to right): Ruby White, Dr. David Eccles, Dr. Olivier Lamiable, Dr. Mark Yang, Dr. Lisa Connor, Rhiannon Sexton, Shiau-Choot Tang, Evelyn Hyde, Prof Franca Ronchese, Elsa Roussel, Kirsty Wakelin (not pictured: Dr. Johannes Meyer, Kerry Hilligan)

Translational Immunology Programme

The 2016–2017 year marked both the end of the Gut Health Research programme and the establishment of the Translational Immunology programme in its place.

The Malaghan Institute is proud to have Dr Olivier Gasser lead this new venture, combining areas of research that will positively impact and support other programmes at the Institute.

HIGH VALUE NUTRITION NATIONAL SCIENCE CHALLENGE

The High Value Nutrition (HVN) National Science Challenge, established in the last financial year, looks at how the microbiome in the gut impacts immunity to infectious agents. Dr Gasser has stepped in to lead the programme, following Professor Elizabeth Forbes-Blom's departure, bringing his range of expertise to the programme.

A positive outcome from this project has been engagement from commercial entities outside the scope of HVN, who have shown interest in the work conducted by Dr Gasser and his team. Dairy-Goat Cooperative has provided funding for a new Research Fellow, helping the laboratory group grow in size and technical expertise.

The next goal of the HVN programme is the application for a second round of funding, which will allow this programme to continue through the 2019–2024 period.

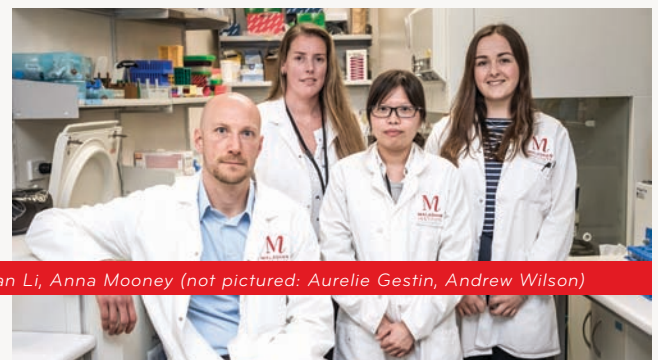
FORWARD-FACING WITH TRANSLATIONAL IMMUNOLOGY

Much of what the Translational Immunology programme aims to answer lies in how the microbiota affects the immune system. Consequently, this work will tie in with wider areas of research and other programmes within the Malaghan, such as asthma and allergy, as well as immune cell biology.

"Where I want to take the science in the next five years is understanding the balance of translocation of metabolites and molecules in the gut," says Dr Gasser. "Our project with the HVN as well as the preclinical models have been

trying to delineate the positive aspects of translocation. Too much is bad, leading to conditions such as leaky gut, but we know that translocation is an essential part of the functional maturation of the immune system.

"Part of the work I've been doing is around looking at the mucosal-associated invariant T cells (MAIT) – immune cells found in mucosal surface in the lung, the gut and skin for example. I'm working to get HRC funding which will align with both Prof Le Gros and Prof Ronchese's programme. If the funding is successful this work will fully overlap with both asthma and allergy as well as the HVN – looking at how the microbiota affects MAIT cell development."



RESEARCH TEAM: (left to right): Dr. Olivier Gasser, Angela Jones, Yanyan Li, Anna Mooney (not pictured: Aurelie Gestin, Andrew Wilson)

Multiple Sclerosis Programme

Professor Anne La Flamme heads the Malaghan Institute's Multiple Sclerosis (MS) programme. Based at Victoria University of Wellington, Prof La Flamme and her team are investigating different ways to treat MS using a variety of new and repurposed techniques, as well as gaining fundamental understanding of this complex disease and its many forms.

CLINICAL TRIAL: MIS416

The MS team has been working with Innate Immunotherapeutics, a New Zealand company that has developed a microparticle which shows potential in use for regulating immune responses.

With the results from this work submitted for publication, this research is looking at how this microparticle harnesses the body's natural reparatory pathways by targeting very specific innate cell types. Of particular promise is the long half-life of this product compared to others, which allows for much longer sustained activation of these innate cells.

"The microparticle has now gone through human clinical trials, and has just completed an exploratory trial," says Prof La Flamme. "We're trying to look at how it affects disease in much larger populations and if there are any correlations with protection with a view to identifying those who may benefit from this treatment."

REPURPOSING OF DRUGS: CRISP CLINICAL TRIAL

In 2016, the CRISP trial recruited its first participants with the goal of determining if clozapine or risperidone, two atypical antipsychotic agents, were suitable to treat progressive MS. The CRISP trial is a randomised, placebo-controlled, blinded clinical trial lead by Dr David Abernethy and the Neurology staff at Wellington Hospital. This ongoing clinical trial has been made possible thanks to the support of Wellington Hospital as well as through funding from MBIE (Ministry of Business, Innovation and Employment) and the Great New Zealand Trek.

The CRISP trial was founded on compelling preclinical work which has been published just this year in *Multiple Sclerosis Journal: Experimental, Translational and Clinical*. This preclinical work identified the therapeutic doses and also looked to see whether these medicines can be used on conjunction with other MS medications, such as glatiramer acetate or "Copaxone", to give additive benefits.

This research demonstrated that these atypical antipsychotic agents modified the disease course within animal models of MS but did not target T cell directly.

A CLOSER LOOK AT PAIN MEDICATION AND MS

In a new avenue of research, Prof La Flamme has been working in collaboration with Dr Bronwyn Kivell at Victoria University of Wellington's School of Biological Sciences. Dr Kivell has been investigating opioid receptors, non-addictive pain medication and their relationship to MS.

Dr Kivell has been working with Prof Thomas Prisinzano, a medicinal chemist in Kansas, on novel compounds to target this system. Thanks to funding received from the Neurological Foundation, the Kate Parkinson's Trust and the Great New Zealand Trek enabling the recruitment of a PhD student, this is a new and exciting avenue for the MS programme.



RESEARCH TEAM: (left to right): Carl Beyers, Katharina Robichon, Sarah Ross, Prof Anne La Flamme, Vimal Patel, Sven Sondhauss, Nikki Templeton (not pictured: Lisa Denny, Isabelle Cornfoot, Augustus Anderson)

Hugh Green Cytometry Core

Through the generosity and support of the Hugh Green Foundation, the Hugh Green Cytometry Core (HGCC) continues to be central to research conducted at the Malaghan Institute.

Increasingly, our scientists are relying on the highly-specialised equipment and expertise of the staff in the HGCC to help their research stand out from the crowd on the international stage.

The main technologies housed in the HGCC include microscopy, flow cytometry and immunohistochemistry, platforms that underpin virtually all research conducted at the Malaghan Institute. This year has seen the acquisition of a new technology platforms that will dramatically expand the scope of data and insight Malaghan scientists are able to gain – improving the quality of our existing experimentation, as well as providing as-of-yet unimagined opportunities for new kinds of research.

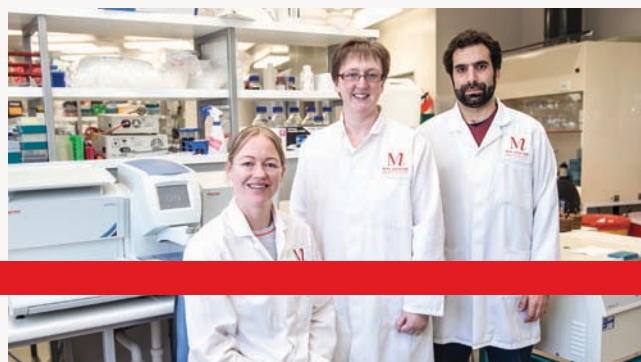
INCUCYTE S3

Microscopy is an essential tool for biological research, medical or otherwise. Another addition to the HGCC has been the installation of a new type of microscope called the 'IncuCyte'. Rather than a traditional microscope that is housed on a laboratory bench, the IncuCyte lives inside a sterile incubator, allowing scientists to track the behaviour and activity of cells as they change over long periods of time, rather than looking through a single snapshot in time as with normal microscopy methods.

"What this means is that we can now culture live cells inside the IncuCyte S3 for weeks or even months, tracking them in real time," says Kylie. "It's brand new technology and we're only just scratching the surface of the different ways we can use it."

"Already we've seen some nice results tracking antigen-specific killing of target cells in realtime. In the past, we've relied on a less accurate intermediate readout of this activity. With the IncuCyte we can be certain that the loss of fluorescence is due to cell death and not any other artefact because we can visualise the cells dying and the dye being released!"

The Malaghan Institute would like to thank the Hugh Green Foundation for their continued support and for the purchase of this instrument.



RESEARCH TEAM: Kylie Price, Sally Chappell, Alfonso Schmidt.

Commercial Development

At the heart of the Malaghan Institute is the desire to bring medical discovery 'from benchtop to bedside' to benefit the health and wellbeing of New Zealanders and the wider population.

Intellectual property is not just about claiming and protecting the discoveries made at the Malaghan Institute – it's an essential component in the sequence of events that transforms early discoveries to viable treatments and cures.

With scientific and medical discovery comes the need to ensure any new intellectual property is filed and patented in a way that enables it to be used in potential therapies. This in turn allows institutes and organisations to attract funders to finance further development and clinical trials. Through commercialisation, treatments that are successful in clinical trials can then make the pivotal leap from the laboratory to the market, where they become available to the wider population.

Without that initial intellectual property and the business entities needed to secure and develop it, medical discovery rarely moves from the benchtop. Establishing organisations and partnerships to protect the commercial side of discoveries and guide them through their lifecycle dramatically increases their chances of getting into the hands of New Zealanders who can benefit from them the most.

WELLINGTON ZHAOTAI THERAPIES

A new joint venture, Wellington Zhaotai Therapies Limited, was formed in May 2017 between the Malaghan Institute and the Hunan Zhaotai Medical Group in Changsha, China. Based on a novel CAR-T cell therapy developed by our Chinese partners, Wellington Zhaotai was formed to capitalise on Malaghan's experience in developing and trialling novel therapies under the highest regulatory standards with a view to taking this therapy to a global market.

With the first CAR-T cell therapies already approved by the FDA, the establishment of the joint venture will be a way to both give New Zealand patients early access to this cutting edge therapy while also developing a new product

in this exciting new market that is owned by a New Zealand company.

An initial timeframe of late 2018 has been set to commence the first round of clinical trials.

AVALIA IMMUNOTHERAPIES

Avalia Immunotherapies was established in 2015 based on intellectual property out of both the Malaghan Institute and the Ferrier Research Institute. These unique compounds were able to demonstrate strong anti-cancer effects through a novel mechanism of action, combining tumour-targeting and immune-stimulating elements in a single compound to elicit powerful anti-tumour responses.

The goal of Avalia Immunotherapies is to develop this technology, which can be applied to a number of cancers and other diseases, and eventually take them to market.

With a recent change to the board of directors, 2017 has signified a different phase in the company's life as it wraps up recent preclinical work and moves towards trialling this therapy in patients.

"There's been a really successful capital raise recently," says Malaghan Institute's Business Development Officer Lucy Pearce. "Right now, Avalia is developing a clinical plan which will allow it to begin its first trial in patients."



General Manager Mike Zablocki and Business Development Officer Lucy Pearce presenting at the 2017 KiwiNet commercialisation awards

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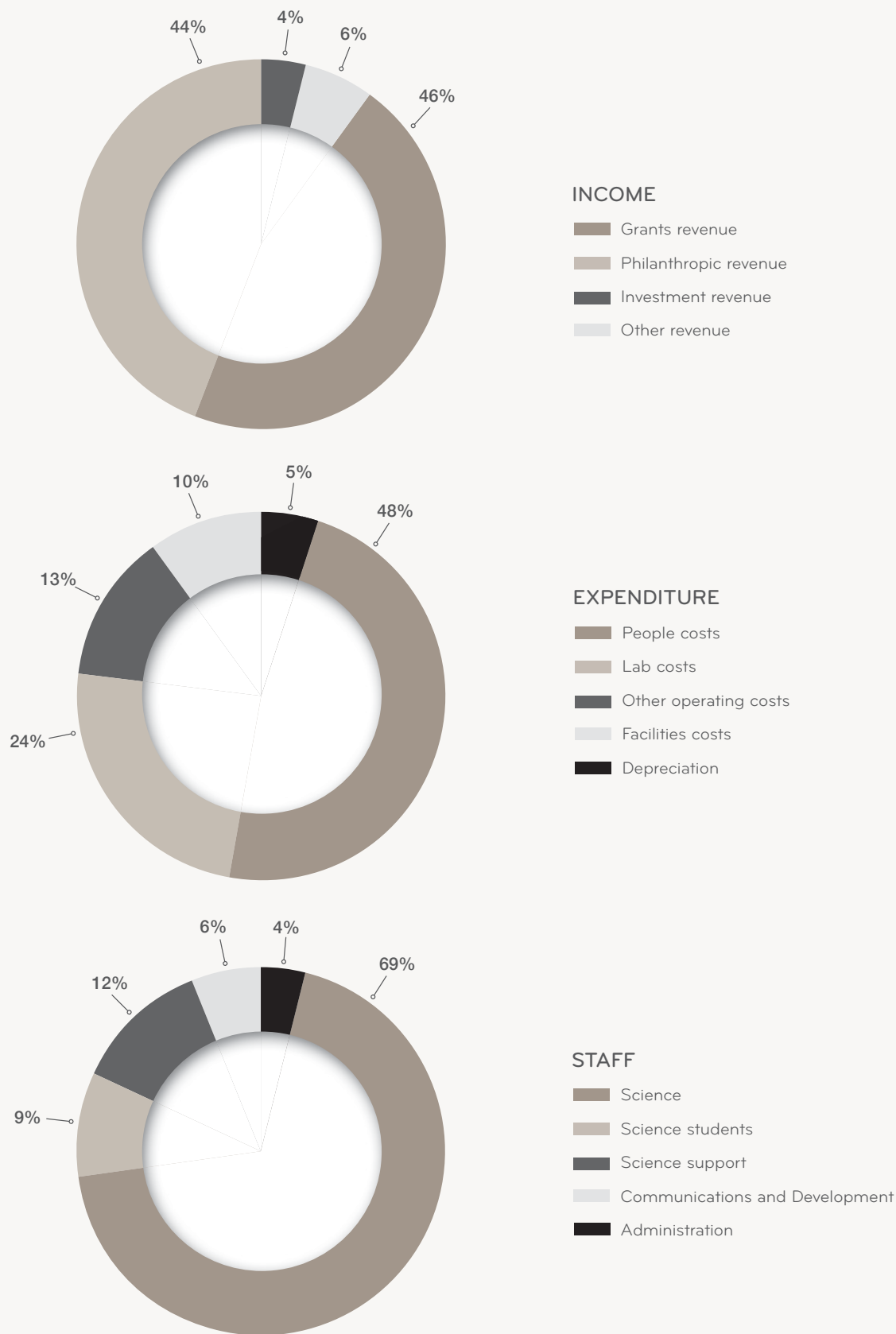
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Financial Overview



FINANCIAL PERFORMANCE

For the year ended 31 July 2017

	2017	2016
	Consolidated	Consolidated
INCOME		
Grants revenue	7,753,381	7,973,588
Philanthropic revenue	7,462,680	2,287,264
Investment revenue	635,655	784,857
Other revenue	973,826	176,598
	16,825,542	11,222,307
EXPENSES		
People costs	5,378,371	4,971,418
Lab costs	2,682,474	2,356,727
Other operating costs	1,482,197	1,257,100
Facilities costs	1,177,905	1,142,931
Depreciation	578,429	529,389
	11,299,376	10,257,565
Share of surplus/(deficit) of associates	(588,791)	-
SURPLUS/(DEFICIT)	4,937,375	964,742

FINANCIAL POSITION

As at 31 July 2017

	2017	2016
	Consolidated	Consolidated
ASSETS		
Current Assets	11,552,956	8,112,935
Non-Current Assets	8,225,605	6,877,916
	19,778,561	14,990,851
LIABILITIES		
Current Liabilities	1,680,887	1,830,553
	1,680,887	1,830,553
NET ASSETS	18,097,673	13,160,299

Funding Sources

We are honoured to receive support from the following organisations, businesses, trusts and individuals.

GRANTS, TRUSTS AND FOUNDATIONS

AgResearch

Albert (Pat) Devine Charitable Trust

Arthur N Button Charitable Trust

BEA Trust

Cancer Society Wellington

Cancer Society, National Body

Carol Tse (No 2) Family Trust

Colin Williamson Charitable Trust

Edith Rose Isaacs Estate

EM Pharazyn Charitable Trust

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Four Winds Foundation

Frimley Foundation

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Joan Fernie Charitable Trust

John Holt Memorial Trust

Keith Seagar Research Fund

Kiwi Innovation Network Limited

Margaret Neave Charitable Trust

Maurice & Phyllis Paykel Trust

Maurice Wilkins Centre

Ministry for Business, Innovation and Employment

Nikau Foundation

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NZ Society for Oncology

Pelorus Trust

Rex & Betty Coker Foundation

SE Leuchars Family Trust

Supreme Grand Royal Arch Chapter of New Zealand

The Claude McCarthy Fellowships

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The David Levene Foundation

The Estates of Ellen, Sinclair, Barbara and Alison Wallace

The Great New Zealand Trek Charitable Trust Inc.

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The Marsden Fund

The Nick Lingard Foundation

The Paddy Brow Charitable Trust

The Rotary Club of Port Nicholson

The Southern Trust

The Thompson Family Foundation

Wellington Medical Research Foundation

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The following people generously left bequests to the Institute:

Carol Anne Bauer

Margaret Baird

Walter Arthur Clark

Valmai Mary Cooke

Beth Donald

Ronald Benjamin Fisher

Walter Freitag

Paul Kingsley Garner

Lois Karen Goodger

Muriel Frances Holder

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Elizabeth Revell

Alison M Reynolds

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Ronald John Thomson

Hilary Ann Willberg

IN MEMORIAM

Gifts were received in memory of the following people:

Heike Adrian

Murray Blackwell

Judith Blair

John Bongiovanni

Robert Boreham

Stephen John Carmine

Graeme Coppell

Elizabeth Molly Davy

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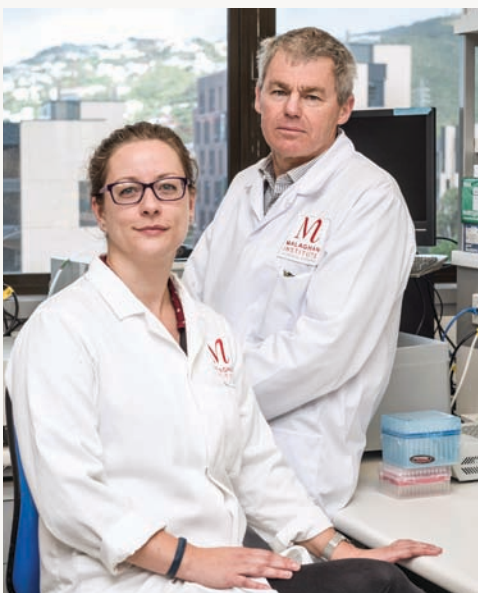
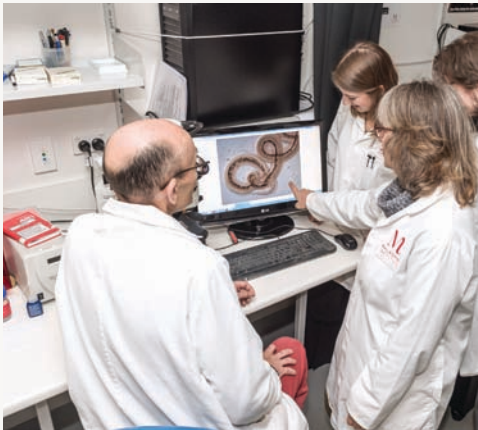
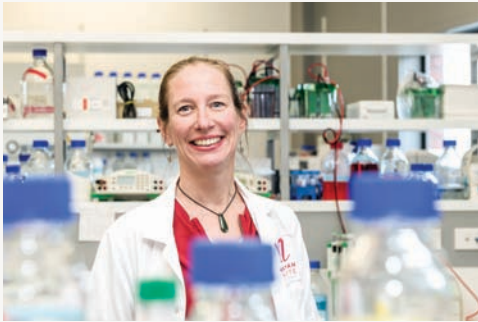
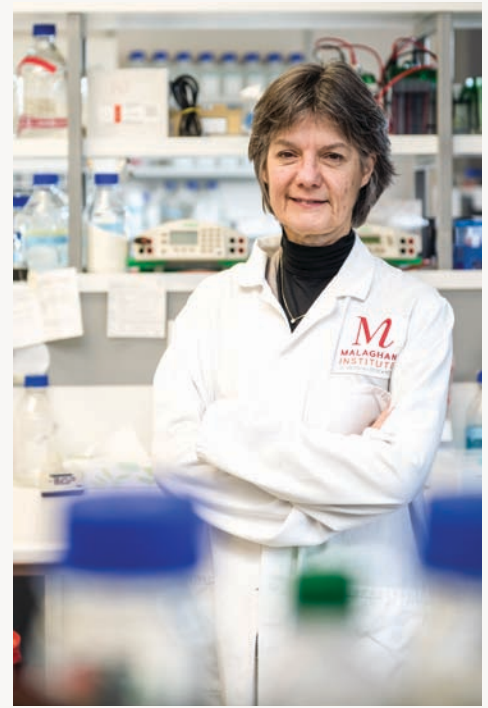
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Dr Elizabeth Forbes-Blom | BSc(VUW), PhD(ANU) – Gut Immunology Team Leader (until Feb 2017)

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

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Jodie Chandler | BBMedSc (Hons) (VUW) – Research Officer

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Emma Petley | BBmedSc(VUW) Masters Student
(To March 2013)

Lucas Pitt | BBmedSc(VUW) - Training &
Operations Manager and Cryopreservation
Manager (BRU)

Dr Hazel Poyntz | BSc(Hons)(Bristol), PhD(Oxford)
- Research Fellow

Dr Nathalie Pujol | PhD - Visiting Researcher (To
July 2017)

Kef Prasit | Bachelor of Arts Psychology, University
of British Columbia, Vancouver, BC, Canada
- PhD Student

Kylie Price | BSc(Otago), MSc(Hons)(VUW) -
Hugh Green Cytometry Core Manager, Head of
Research Technology

Melanie Prout | BSc(Hons)(VUW) - Senior
Research Officer

Elsa Roussel | Research Officer (until July 2017)

Ian Saldanha | BSc, PGDipSci(Otago),
DipVetNursing(Otago Polytech) BRU Manager

Alfonso Schmidt | BSc(Chile) - Staff Scientist

Dinindu Senanayake | BBmedSc (VUW) -
Research Officer in Bioinformatics (until Oct 2016)

Rhiannon Sexton | BSc Biomedical Science,
Victoria University - Master's Student

Sonali Sharma | BSc(Hons) (HPU), MSc (SUBMS)
- Animal Technician

Dr Mary Speir | PhD, Monash University -
Postdoctoral Research Fellow (until Dec 2016)

Adam Stewart | BSc(VUW) - Senior Animal
Technician

Shiau-Choot Tang | Grad Dip Sci(VUW) - Senior
Research Officer

Ching Wen Tang | MSc(Otago) - Senior Research
Officer

Dr Lieke Van Den Elsen | BSc, MSc, PhD (Utrecht)
- Research Fellow (until Jan 2017)

Kirsty Wakelin | BBiomedSc (Hons) (Otago) -
Research Officer

Dr Xiaodong Wang | Dip Med Tech, Dip
Midwifery(Shanxi) - Senior Animal Technician

Ruby White | BSc(Hons) (Otago) - Research
Officer (To June 2017)

Andrew Wilson | BBMedSc (VUW) - Masters
Student

Catherine Wood | RN, BN, MHSc -
Clinical Research Coordinator (until Feb 2017)

Dr Jianping (Mark) Yang | BM(Shanxi) - Senior
Research Officer

Tingli Yang | BBmedSc(Auckland) - Animal
Technician (until Feb 2017)

Bibek Yumnam | MSc (Tezpur, India) - Animal
Technician Genetic Quality Specialist

Dr Deepa Patel | BSc(Hons), PhD (Auckland) -
Postdoctoral Research Fellow

SUPPORT AND ADMINISTRATION

Marie Armstrong | BAP - IT Manager

Elliott Caldwell | Cisco Diploma of Computer
Networking (CCNA) at Christchurch Polytechnic
Institute of Technology IT Support Technician
(part-time)

Sally Culbert | BBS - Finance(Massey) -
Management Accountant (Part-Time)

Tim Dallas | Assistant Facilities Manager

Gabrielle Dennis | RSA(English), Pitmans - HR and
Admin Officer (part-time) (until May 2017)

Charlie Holland | BA(Hons) (Waikato), MA (VUW)
- Community Fundraising Manager

David Lin | CA(NZICA), MBA(VUW), MAF(VUW)
- Finance Manager

Yvonne Mackie | Funding Administrator

Kathleen Martsch | MA (Merit) International
Business and Management, University of Bradford,
UK - Communications and Marketing Manager
(to June 2017)

Maree O'Connor | Diploma Business Studies,
DipMgt New Zealand Institute of Management
- Assistant Accountant (part-time) (from Nov 2016)

Nicola Olson | CA(NZICA), BCA(VUW), BA (VUW)
- Financial Accountant (part-time)

Lucy Pearce | BSc(Otago) - Business Development
Officer

Aidan Pedley | Fundraising Administrator
(part-time) (until Aug 2017)

Lene Petersen | Accounts Payable (part-time)
(from June 2017)

Ilse Potes Morales | BMktg & Advertising (U. San
Martin) (Colombia) - EA to Director & General
Manager

Raewyn Roberts | TTC (Distinction) Trained
Teachers Certificate Funding Manager Auckland
(part-time) (from June 2017)

Tony Robinson | BA (Cantab), MA (Hons)
Aberdeen, PGCE (Oxford) - Funding Manager

Jennifer Sheil | Msc Science Communication
(Otago NZ) - HR & Research Office Advisor (from
May 2017)

Jenny Sim | Development Manager

Darrell Smith | MSc(Hons)(VUW), BSA(Massey)
- Facilities Manager (part-time)

Jo Timewell | Facilities Assistant (From Oct 2016)

Apii Ulberg | Cleaner (from June 2017)

Laura Van Til | BSc - Casual Science Writer

Nicholas Walshe | HR & Research Office Manager

Mike Zablocki | BA(Hons)(Bristol), PGDipBA(VUW)
- General Manager

Hamish Cameron | BSc(Tech)(Waikato) - Science
Communicator



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