Walter+Eliza Hall
Institute of Medical Research

# Annual Report
2010-2011

**Mastery of disease through discovery** | www.wehi.edu.au

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## The Walter and Eliza Hall Institute of Medical Research

**1G Royal Parade**
**Parkville Victoria 3052 Australia**
**Telephone: (+61 3) 9345 2555**
**Facsimile: (+61 3) 9347 0852**

## WEHI Biotechnology Centre

**4 Research Avenue**
**La Trobe R&D Park**
**Bundoora Victoria 3086 Australia**
**Telephone: (+61 3) 9345 2200**
**Facsimile: (+61 3) 9345 2211**

**www.wehi.edu.au**
**www.facebook.com/WEHIresearch**
**www.twitter.com/WEHI_research**

**ABN 12 004 251 423**



## Acknowledgements

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## Cover image

**Art in Science finalist 2010**
Vessel webs
**Dr Leigh Coultas**, Cancer and Haematology division

This image shows the delicate intricacy in the developing eye of a transient population of web-like blood vessels. The cells in the vessels will be depleted during development in a regulated process called apoptosis, or programmed cell death. Tumours frequently recruit and develop extensive blood supplies to help them grow. Scientists from our Cancer and Haematology division are investigating ways of killing tumours by inducing apoptosis. The mechanisms that cause apoptosis in the cells pictured may be useful in understanding how we can induce apoptosis in tumour blood vessels, effectively killing cancer cells by starving them of their blood supply.

# About the institute

## Our mission

**Mastery of disease through discovery**

## Our vision

**To be an innovative medical research institute that engages and enriches society and improves health outcomes through discovery, translation and education.**

## Research themes

**CANCER | CHRONIC INFLAMMATORY DISEASE | INFECTIOUS DISEASE**

## Key objectives

| | |
|---|---|
| **Discovery** | **to make discoveries in medical biology that shape contemporary thinking and paradigms and enhance the understanding and treatment of disease** |
| **Translation** | **to convert our discoveries into improvements in disease diagnosis, prevention and treatment** |
| **Education** | **to develop and enrich the skills and experience of students and staff, allowing each person to realise their potential and contribute to a vibrant campus** |
| **Engagement** | **to engage with the community and develop support for medical research generally and the institute's mission specifically** |
| **Sustainability** | **to build an infrastructure, funding and research capacity that enables the institute to fulfil its mission in a sustainable manner** |

An interior view of the new western wing of the institute (below left) and an exterior view of the front of the building (below right).

**The Walter and Eliza Hall Institute is home to more than 650 researchers who are working to understand, prevent and treat diseases including cancer – particularly blood cancers and breast cancer; chronic inflammatory diseases such as type 1 diabetes, rheumatoid arthritis and coeliac disease; and infectious diseases such as hepatitis and malaria.**

**It is committed to making fundamental discoveries about the way cells, particularly cancer and blood cells, behave and communicate and seeing these discoveries translated into benefits for patients.**

**The institute was founded in 1915 as a benevolence of the Walter and Eliza Hall Trust to be 'the birthplace of discoveries rendering signal service to mankind in the prevention and removal of disease and the mitigation of suffering'.**

**It is affiliated with The University of Melbourne and The Royal Melbourne Hospital. It offers postgraduate training as the Department of Medical Biology of The University of Melbourne.**

## Director
**Douglas J Hilton**
BSc *Mon* BSc(Hons) PhD *Melb* FAA

## Deputy Director
**David Vaux**
MB BS BMedSc PhD *Melb* FAA

## General Manager
**Maureen O'Keefe**
BSc(Hons) *Mon* DipEd MBA *Melb*
GAICD WCLP

## Company Secretary
**Murray Jeffs**
BBus(Accounting) *RMIT*
CPA FCIS SF Fin

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FRCPA FRACOG(Hon) FRCPath
FRACGP FRSE FTSE FAA FRS

Dr Matthew Call and Dr Melissa Call (below left) jointly manage a laboratory in the Structural Biology division.

Dr Thomas Nebl (below right) has recently joined the institute's Systems Biology and Personalised Medicine division.

# Director's and Chairman's report

**Although we are only part-way through our building and renovation program, which is due to be completed in November 2012, the past 12 months have seen some major milestones being met, most notably the completion of the new western wing of the building and the relocation of many of our researchers into this state-of-the-art facility.**

Two aspects of this project have been particularly pleasing. First, we have been able to deliver this part of the project on time and under budget, and hence have been able to commit to fully renovating the east wing of our building. Second, occupation of the building proceeded exceptionally smoothly, with our scientists performing experiments within days of moving. We look forward to the completion of this project and the building's formal opening in 2012, and thank the Australian and Victorian Governments, The Atlantic Philanthropies, The Ian Potter Foundation, the Australian Cancer Research Foundation, the Drakensberg Trust and numerous other donors and supporters for supporting this major project.

The institute's centenary in 2015 is rapidly approaching, giving us the opportunity to reflect on our history and our current position. Eliza Hall's vision for the institute was that it should "be the birthplace of discoveries rendering signal service to mankind in the prevention and removal of disease and the mitigation of suffering".

Our researchers have made Mrs Hall's vision a reality: from Sir Charles Kellaway's production of anti-venom in the 1930s, to Sir Macfarlane Burnet's Nobel Prize-winning theory of clonal selection in the 1950s, and Professor Don Metcalf's discovery of colony stimulating factors in the 1960s, which not only revolutionised haematology, but over the past 20 years has helped more than 10 million cancer patients complete their chemotherapy with reduced risk of infection.

Institute director Professor Doug Hilton (below left) with board president Mr Leon Davis

In the past 12 months we have added to this legacy.

Our scientists have made many fundamental discoveries, including the visualisation of the malaria parasite in 'super resolution'; elucidating the role that the major human cancer-causing gene *ERG* plays in stem cell self-renewal; the demonstration that parasitic worms use the same family of cell survival proteins as human cancer cells; and that the blood cell hormone interleukin-7 can boost the response to human viral pathogens such as HIV, hepatitis B and hepatitis C, which are major health burden globally.

On the translational side there is also much excitement and anticipation. Australian cancer patients are benefiting from the 20 years of effort invested by more than 100 institute scientists in unravelling the mysteries of cell death and cell survival. This collaboration has involved molecular and cell biologists, medicinal chemists, structural biologists, clinicians and nurses – in short, the full spectrum of research talent at the institute and in our precinct partners. Because of our deep understanding of this area of biology, two major international pharmaceutical companies, Abbott and Genentech, a member of the Roche group, have chosen to collaborate with us to help develop pharmaceuticals which target proteins that give cancer cells a survival advantage. This means that cancer patients at The Royal Melbourne Hospital are among the first in the world to benefit from these new designer therapies.

The first of these new compounds, navitoclax, is now in phase II clinical trials, while the second, ABT-199, which was co-developed by chemists and structural biologists at the institute, is in phase Ia trials in patients with chronic lymphocytic leukaemia who have not responded to conventional treatment. Equally exciting are the three different vaccine approaches that have emerged from our research efforts into malaria over the past 20 years, which are now in clinical trials in humans, as well as the ongoing clinical development of preventive approaches for diabetes and coeliac disease.

If new treatments and new technologies are going to have maximum impact on disease prevention, diagnosis and treatment, the Australian community must embrace health and medical research. We have been overwhelmed by the support we have received from the community, not only during the 'Discoveries Need Dollars' campaign that preceded the federal budget in May, but also in response to stories about our work that have appeared in the print media, radio, television and online. We are also immensely proud of the role played by our animators, Mr Drew Berry and Ms Etsuko Uno, who take complex biomedical ideas and turn them into highly informative, accessible and beautiful animations. Their work has been downloaded from YouTube hundreds of thousands of times; displayed in art galleries and museums, including the Museum of Modern Art in New York; received a British Academy of Film and Television Arts award and this year was recognised by a Macarthur Fellowship (also known as the Genius Award) to Mr Berry.

Funding and donations have again played a major role in supporting the work of our institute. We are truly grateful for support we have received from governments and donors this year. It has made all our work possible and allowed us to develop young talent which will underwrite our future research.

We have no doubt that when future leaders and supporters of the institute reflect on this period, that they will recall a halcyon time. We thank you for being part of the Walter and Eliza Hall Institute family and trust you will take much pride in the achievements of our staff and students.

## Remembering Frank Fenner 21.12.1914 – 22.11.2010

**Last year, institute staff mourned the loss of one of the great minds of Australian science, acclaimed virologist and microbiologist Professor Frank Fenner.**

Professor Fenner was best known for his work in eradicating smallpox and for his studies of the myxomatosis virus, used to control rabbit plagues from the 1950s.

For a short but influential time in the late 1940s, Professor Fenner worked at the Walter and Eliza Hall Institute. Professor Fenner was recruited by then director Sir Macfarlane Burnet to work on Ectromelia, or mousepox as they later called it.

Professor Fenner and Sir Macfarlane Burnet showed that mice could be vaccinated against mousepox with vaccinia virus, another poxvirus historically used to vaccinate humans against smallpox. They remained close friends, and co-authored *The Production of Antibodies*, a key publication in immunology that outlines Burnet's seminal ideas about 'self' and 'non-self' in the immune system.

Professor Fenner's work at the institute cemented his interest and involvement in virology, particularly poxviruses, which were to be his lasting legacy and contribution to science and human health.

Professor Phil Hodgkin, head of immunology at the institute, worked with Professor Fenner at the John Curtin School of Medical Research during the 1980s and 1990s.

He remembers Professor Fenner as an "incredibly generous scientist". "We always felt very privileged to be in his company, to hear his stories and to be guided by his wisdom and experience," Professor Hodgkin said. "He just loved finding out everything he could about a subject and imparting that to as wide an audience as he could. He was an inspiration for generations of scientists and epitomised the dedicated humanitarian academic."

Professor Frank Fenner

# Discovery

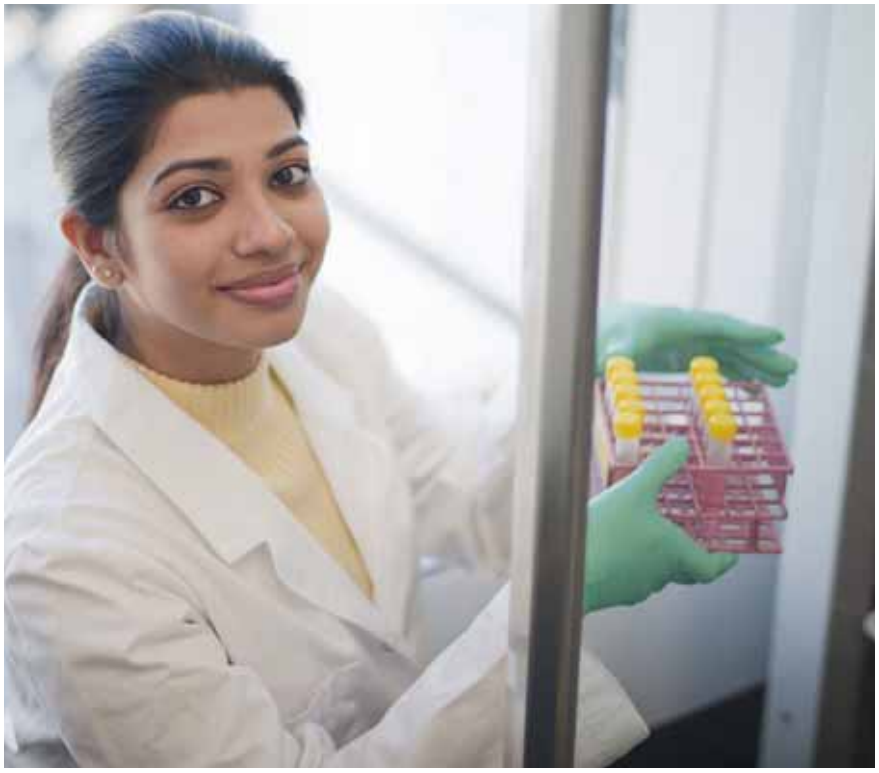
PhD student Ms Sarah Best, from the Stem Cells and Cancer division, is seeking to better understand the role of particular proteins in mammary gland development.

# Discovery

**Collaborative and multidisciplinary research has long been a strength of the Walter and Eliza Hall Institute. Although our research groups are clustered in divisions to reflect common interests, research collaborations span divisions and many of our most important discoveries have been the outcome of cross-disciplinary, cooperative efforts. Our researchers are united towards improving human health, focusing on cancer, chronic inflammatory disease and infectious diseases.**

As part of the institute's expansion, which began in early 2009, a reorganisation of the research divisions has been undertaken to better reflect the core research interests of our scientists and the institute's strategy. This resulted in the formation of three new divisions in 2011 – Cell Signalling and Cell Death, Inflammation, and Molecular Immunology. In addition, the division of Stem Cells and Cancer was established in 2010, and a new division of Systems Biology and Personalised Medicine will begin in July 2011. As part of the reorganisation, the division of Autoimmunity and Transplantation ceased operations in December 2010, with the reassignment of researchers to allied divisions.

Contemporary biology requires researchers to integrate data from diverse fields, including genomic, proteomic, cell-based and statistical analyses. The institute supports the ongoing research activities of our scientists by providing access to advanced technologies and by promoting collaboration between specialists in distinct fields, and encouraging researchers to develop skills in diverse areas. As the following pages demonstrate, our successes in the past year have stemmed from a strong collaborative, cross-divisional approach that sees our research discoveries span from basic science to translational research.



PhD student Ms Sweta Iyer (below left) is investigating how the proteins Bak and Bax insert into the mitochondrial membrane, leading to programmed cell death.

Dr Nai Yang Fu (below right) is looking for the genes that may be behind some breast cancers.

## Understanding the role of the Bcl-2 family in health and disease

It is more than 20 years since institute researchers identified the role of the Bcl-2 protein family in preventing the death of leukaemia cells, and the subsequent discovery of the role of Bcl-2 in programmed cell death. Since then, the combined efforts of our researchers have resulted in important discoveries about the function of Bcl-2 and related molecules and their relevance to health and disease. In 2011 this resulted in the start of phase Ia clinical trials of a potential new BH3-mimetic inhibitor of Bcl-2, called ABT-199 (GDC-0199/RG7601), for the treatment of chronic lymphocytic leukaemia, the most common type of leukaemia. ABT-199 was discovered and developed through a three-way collaboration between scientists in the institute's Chemical Biology division and pharmaceutical companies Abbott and Genentech, a member of the Roche Group. The entry of ABT-199 into clinical trials highlights the institute's ability to translate basic discoveries into potential new therapies for human disease.

The Bcl-2 family is also important in other diseases. Scientists in our Autoimmunity and Transplantation, Stem Cells and Cancer, and Bioinformatics divisions have revealed the potential for inhibitors of Bcl-2 family members to be used to treat rheumatoid arthritis and breast cancer. Research from the Molecular Genetics of Cancer, and Cancer and Haematology divisions has shown the importance of Bcl-2-like proteins in the formation of blood vessels that supply nutrients to solid tumours. These are all exciting developments that have the potential to be developed into new treatments for these diseases.

Our scientists also remain committed to basic research into the biology of the Bcl-2 family. Research from the Immunology, Inflammation, Molecular Genetics of Cancer and Molecular Immunology divisions has defined which Bcl-2-like proteins are required for the development and maintenance of specific T and B cell subsets. Scientists in the Cell Signalling and Cell Death division are elucidating how some Bcl-2-like proteins function to initiate cell death. Another important advance has been the determination, by researchers in the Structural Biology division, of the crystal structures of Bcl-2-like molecules bound to natural and pharmacological inhibitors. This information will be especially important for advancing the design of new inhibitors of Bcl-2 family members, which could lead to new potential therapies for cancer.

## New ways to treat infectious diseases

Improving treatments for infectious diseases has been a focus of the institute since its founding. In 2010-2011 our scientists have made important discoveries that have revealed new strategies for combating viral and parasitic diseases.

Scientists in the Infection and Immunity division have demonstrated that the cell signalling molecule interleukin-7 (IL-7) has the potential to boost the immune response to fight persistent viral infections in mice. This opens up new avenues for treating chronic infectious diseases in humans including HIV and hepatitis B and C, which are significant disease burdens in developing nations.

Parasitic diseases are another focus for our scientists. Research from the Structural Biology and Bioinformatics divisions has revealed that the parasite that causes schistosomiasis expresses Bcl-2-like molecules. This raises the possibility that modulation of the Bcl-2 family may be a novel option for treating parasitic diseases. Research into the biology of the malaria-causing *Plasmodium* parasite by scientists in the Infection and Immunity division continues to reveal potential new drug targets for treating malaria. Major achievements in this field in the past year have included the discovery of a new family of proteins required by the parasite to recognise red blood cells, and, for the first time, the visualisation of the parasite invasion process in molecular detail. This information is being used by researchers in the Chemical Biology division to discover new antimalarial compounds in a high-throughput chemical screen.

## Silencing the immune response to treat disease

Chronic inflammatory diseases such as type 1 diabetes and rheumatoid arthritis put immense strain on health systems worldwide. Our researchers have made significant advances in determining how to diminish the immune response as a means of treating or preventing these diseases. Scientists in the Autoimmunity and Transplantation, and Immunology divisions have developed vaccines that are currently in clinical trials. An intranasal vaccine has been developed for preventing type 1 diabetes by stimulating tolerance to insulin, while another vaccine currently being trialled aims to cure coeliac disease through desensitisation to proteins in gluten.

Institute scientists have also advanced the understanding of the cellular and molecular mechanisms that drive inflammation. The Inflammation division is investigating the role of secreted molecules in controlling inflammatory cells. Meanwhile, scientists in the Molecular Immunology division have defined a subset of white blood cells that are important for suppressing the immune response. These discoveries could lead to new strategies to combat inflammatory diseases in the future.

HIV researchers Dr Marc Pellegrini (above left) and Mr Simon Preston

# Cancer and Haematology

**Leukaemias and autoimmune disorders develop when the mechanisms controlling normal blood cell proliferation and function are subverted.**

The Cancer and Haematology division aims to discover the molecules that control these regulatory processes with the ultimate goal of devising new strategies for fighting disease. We work collaboratively with other institute divisions, particularly Molecular Medicine and Inflammation, and have strong links with clinical and commercial partners for research translation.

Our researchers use rapidly-evolving genomics tools to discover novel regulators of blood cell production and function. Recent discoveries in this area have highlighted the important role and intricate regulation of blood stem cells, the rare bone marrow cells responsible for lifelong blood cell production, which often develop disease-causing mutations. Our studies of the c-Myb and Erg transcription factors have revealed novel mechanisms via which stem cells sense and respond to the number of mature blood cells, as well as how stem cell functions are differentially controlled under normal and stress conditions.

Originally discovered in our division, the blood cell hormones (cytokines) control the number and function of blood cells, and have been used to treat patients with low white blood cell numbers, which often result from cancer therapy. To improve treatment, as well as design new therapies for inflammation and cancers, we continue to explore the mechanisms of cytokine action. Recent research highlights include the discovery by Dr Jeff Babon of a novel biochemical mechanism by which the Suppressors of Cytokine Signalling (SOCS) proteins switch off cellular responses to cytokines, which has important implications for the design of inhibitors of cytokine action (see opposite page).

We also welcomed the appointment of new laboratory heads whose skills and research activities enrich and extend the division's program. Dr Emma Josefsson, who studies regulation of platelet production and function, will continue this research theme and explore the roles of platelets in cancer. Dr Matthew McCormack brings an exciting program of research into leukaemia-causing genes and leukaemia stem cells, and Dr Samir Taoudi, appointed jointly with the Molecular Medicine division, whose research is unlocking the mysteries of how the blood cell system develops.

## Laboratory heads

**Professor Warren Alexander**
Division head

**Dr Jeff Babon**

**Dr Emma Josefsson**

**Dr Benjamin Kile**

**Dr Graham Lieschke**

**Professor Donald Metcalf**

**Dr Matthew McCormack**

**Professor Nick Nicola**
Division head

**Dr Samir Taoudi**

**Professor Andrew Roberts**


Dr Jeff Babon (below left) and Professor Nick Nicola are studying the interactions of internal cell signalling proteins called Janus kinases.

## Cell signalling discovery provides new hope for treating blood disorders

**Myeloproliferative diseases are serious blood disorders that cause an excessive number of blood cells to accumulate in the bone marrow. They can be severe and are sometimes fatal.**

Dr Jeff Babon, Professor Nick Nicola and colleagues from the institute's Structural Biology and Cancer and Haematology divisions have spent many years studying the interactions of internal cell signalling proteins called Janus kinases (JAKs). JAKs are activated in response to blood cell hormones called cytokines and are essential for maintaining the blood system and for instructing immune cells to respond to infection and inflammation.

Dr Babon said mutations in one particular molecule, JAK2, are strongly associated with the development of myeloproliferative diseases. "When JAK2 is mutated, it tells the cell to continually multiply, or proliferate. An excessive amount of blood cells of one type are produced, and the bone marrow is overrun, leading to problems with production of other essential cell types and eventually bone marrow failure," he said.

Dr Babon investigates the interaction between JAK2 and the inhibitory SOCS (Suppressors of Cytokine Signalling) proteins. SOCS were discovered at the institute in the 1990s and provide a necessary 'negative feedback' response that stops JAK2 becoming overactive.

"SOCS3 is a key inhibitor of JAK2 proteins in blood and immune cells, but we didn't know exactly how the two proteins interacted to suppress JAK2 function," Dr Babon said. "In our research, we were interested in identifying which site the SOCS3 protein bound to on the JAK2 protein to inhibit its action. We were surprised to find that SOCS3 binds to a unique site on JAK2, and directly inhibits the protein, rather than out-competing other molecules."

He said the finding could inspire a new class of therapeutic agents for treating myeloproliferative diseases. "The SOCS3 binding site is a previously unknown part of JAK2 which could be exploited as a drug target, with greater specificity than other drugs that are currently in clinical trials for inhibiting JAK2," he said.

**Collaborating organisations:** Monash University and The University of Melbourne.

**Funding partners:** National Health and Medical Research Council, National Institutes of Health (US), and the Victorian Government.

**More information:** Presented at the 39th Annual Scientific Meeting of the Society for Hematology and Stem Cells, Melbourne, 15-18 September 2010.

## Advancing medical research through better microscopes

**Microscopy is a vital tool in medical research, and recent advances in technology have provided scientists with new and more detailed views into cells and tissues.**

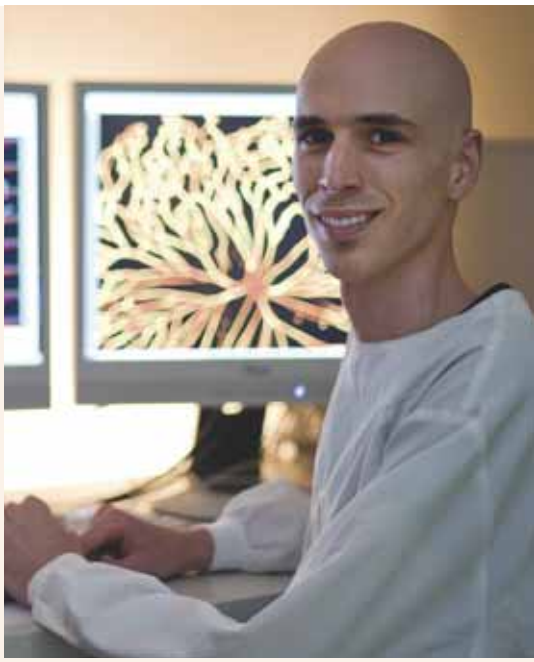
A donation of almost $25,000 by The Jack Brockhoff Foundation has allowed institute researchers to capitalise on these advances by enabling an upgrade of our Zeiss LSM 5 Live microscope.

The upgrade means institute microscope users can now create highly-detailed images of whole organs, using up to four separate fluorescent markers. Dr Leigh Coultas from the Cancer and Haematology division used the microscope to produce the image on the cover of this annual report: a blood vessel network in the developing eye.

"Often, it is only by visualising an entire sample in high resolution that we can get an accurate picture of what is happening in biology," said Dr Coultas, who is studying the control of cell death in the blood vessel lining.

"In this case, we need to see the entire sample to be able to accurately count the number of blood vessels in it," he said. "We are using this information to determine the role of different genes in blood vessel cell death. This research may provide clues for killing tumour-associated blood vessels, thereby starving the tumour of its blood supply."

The head of the institute's Imaging Facility, Dr Kelly Rogers, said the upgraded microscope would benefit many research projects. "There is high demand for fluorescent microscopy from our scientists," she said. "As well as the studies of blood vessel regulation, the upgraded microscope has been used to gain insights into how malaria parasites invade red blood cells, and how autoimmunity develops."



Dr Leigh Coultas produced the extraordinary image on the cover of this year's annual report with the institute's upgraded microscope. The microscope upgrade was made possible by a donation from The Jack Brockhoff Foundation.

# Stem Cells and Cancer

**The Stem Cells and Cancer division studies the normal development of epithelial tissues and organs, and cancers arising within them.**

Epithelial organs are those that primarily consist of epithelial cells – such as skin, breast, ovary and lung. Cancers of epithelial cells (carcinomas) account for approximately 80 per cent of cancers and are major causes of death and disease worldwide, yet improved treatment strategies have only resulted in modest improvements in cancer survival.

Our division is focusing on breast, ovarian and lung cancers, with the key objective of understanding the normal development of these organs and which cell types within them are predisposed to cancer.

In the breast cancer laboratory we have made significant inroads into identifying the different types of epithelial cells that reside in breast tissue. Recent studies have revealed that breast stem cells are highly responsive to the hormones oestrogen and progesterone, despite lacking receptors for these hormones. Our laboratory unravelled the cellular mechanism that accounts for the link between sustained exposure to female hormones and increased breast cancer risk. We identified, through gene expression profiles, which genes in epithelial cells are affected by hormone actions, including the RANK signalling pathway. Current work is addressing whether blocking this pathway can prevent breast cells becoming cancerous, or inhibit tumour growth.

We are also investigating genes that regulate mammary gland development in order to understand how changes to these genes could contribute to cancer development. Analysis of different mouse models of breast cancer and human breast tissue has revealed potential 'cells of origin' of cancer. We are also undertaking studies that have the potential to identify molecules that could serve as novel prognostic markers or therapeutic targets in breast cancer.

Similar approaches are being applied to studying ovarian and lung cancers. Ovarian cancer usually presents at a late clinical stage and is often resistant to existing therapies. The most lethal type is high-grade serous ovarian cancer. To better understand this aggressive form of cancer we are generating preclinical models of disease to test new treatments. Studies in the lung cancer laboratory are also centred on establishing a bank of lung cancer models representative of different cancer subtypes.

## Laboratory heads

**Dr Marie-Liesse Asselin-Labat**

**Professor Geoff Lindeman**
Division head

**Associate Professor Clare Scott**

**Professor Jane Visvader**
Division head

Professors Jane Visvader (below left) and Geoff Lindeman believe that BH3-mimetics could hold promise for treating aggressive breast cancers.

## Anti-cancer agents show promise for aggressive breast cancers

**Triple negative breast cancers account for up to 20 per cent of all breast cancers and are typically aggressive with a poor prognosis.**

They are called triple negative cancers because they test negative for the oestrogen, progesterone and HER2 receptors, and cannot be treated with hormone therapy or drugs that have been useful in treating other forms of breast cancer.

Researchers from the institute have found that some of the most aggressive forms of breast cancer are more vulnerable to chemotherapy when the chemotherapy is combined with a new class of anti-cancer agent.

Professors Geoff Lindeman and Jane Visvader, who led the research with colleagues Drs Samantha Oakes and François Vaillant, said that a new class of anti-cancer agents called BH3-mimetics showed promise for treating breast cancers, including triple negative cancers.

BH3-mimetics target and neutralise the so-called Bcl-2 proteins in cancer cells. Bcl-2 proteins act to 'protect' the cells after they have been damaged by chemotherapy drugs, and prevent the cancer cells from dying.

The BH3-mimetic compound ABT-737 targets proteins from the Bcl-2 family, which are found at high levels in up to 70 per cent of breast cancers, Professor Lindeman said. "We have shown that breast tumours that have high levels of Bcl-2 respond well to treatment with ABT-737 when used in combination with a conventional chemotherapy drug," he said.

Professor Visvader said combined treatment with ABT-737 and docetaxel (a chemotherapy drug commonly used for treating breast cancer) in mice transplanted with human breast cancer cells improved tumour response and survival rates, when compared to docetaxel as a single agent.

Professor Lindeman said early results suggest navitoclax (an orally-deliverable BH3-mimetic which is an analogue of ABT-737) could provide new hope for treating some breast cancers that are not candidates for other currently available treatments. Navitoclax is being jointly developed by pharmaceutical companies Abbott and Genentech, a member of the Roche Group.

"The research suggests that these BH3-mimetic agents make the cancer cells more vulnerable to chemotherapy," Professor Visvader said. "We are particularly excited about using this combination to treat Bcl-2-expressing breast cancer, including basal-like breast cancer, which is often the hardest to treat."

**Funding partners:** Australian Cancer Research Foundation, National Breast Cancer Foundation, National Health and Medical Research Council, Victorian Breast Cancer Research Consortium, Victorian Cancer Agency, Victorian Cancer Biobank, and the Victorian Government.

**More information:** Oakes SR, Vaillant F, Lim E, Lee L, Breslin K, Feleppa F, Deb S, Ritchie ME, Takano E, Ward T, Fox SB, Generali D, Smyth GK, Strasser A, Huang DC, Visvader JE, Lindeman GJ. Sensitization of BCL-2-expressing breast tumors to chemotherapy by the BH3 mimetic ABT-737. *Proceedings of the National Academy of Sciences USA*. 2011 Jul 18; doi: 10.1073/pnas.1104778108

## L'Oréal Fellowship winner seeks to understand cancer

**A desire to understand how breast cancer starts saw institute researcher Dr Marie-Liesse Asselin-Labat win one of three 2010 L'Oréal Australia For Women in Science Fellowships.**

The L'Oréal Fellowships are awarded to female early career scientists to reward research excellence and support their rise to leadership positions in science.

Dr Asselin-Labat from the institute's Stem Cells and Cancer division received the $20,000 L'Oréal Fellowship for her research into breast stem cells and their role in some types of breast cancer. She was part of the institute team that identified breast stem cells, a discovery that caused a major shift in the way scientists thought breast cancer developed. The team also revealed that oestrogen and other female hormones can control the function of breast stem cells.

In 2011 Dr Asselin-Labat established her own laboratory in the Stem Cells and Cancer division, focusing on lung cancer. "I'm interested in looking at how lung stem cells are regulated and what drives tumour initiation in the lungs," Dr Asselin-Labat said.

"Our laboratory intends to use the discoveries into breast stem cells and their role in breast cancer to further our understanding of how lung cancer develops. There is a real need for research into lung cancer, because remarkably little is known about how it develops and the cells that are at the origin of the cancer."

Dr Asselin-Labat said the L'Oréal Fellowship had allowed her to get laboratory assistance to maintain productivity, helped with childcare costs, and supported her participation in leadership training.

Dr Marie-Liesse Asselin-Labat

# Molecular Genetics of Cancer

**Normal cells in our bodies have a limited lifespan and those that are damaged, potentially dangerous, or no longer needed are eliminated by a process of programmed cell death called apoptosis.**

A cell that develops a defect in its apoptosis machinery will fail to die when it should and may multiply to give rise to cancer. Further, defective apoptosis makes cancer cells resistant to the chemotherapy and radiation interventions commonly used to treat cancer.

Our division is exploring how apoptosis is controlled and how disruptions in this vital cellular process lead to cancer and limit the effectiveness of current therapies. Importantly, our increased understanding of apoptosis has galvanised the search for novel drugs that directly trigger the apoptotic machinery to kill cancer cells.

One of the two distinct pathways to apoptosis is triggered when 'death receptors' on the cell surface are engaged by protein ligands that bind specifically to these receptors. The other pathway is triggered when various stress stimuli produce signals inside the cell that act upon the Bcl-2 protein family; the resulting tussle between opposing factions of this family determines whether the cell lives or dies. The process is controlled by three forces: Bcl-2 and the other pro-survival family members restrain their pro-death relatives Bak and Bax until the apoptosis-initiating 'BH3-only' proteins issue the death warrant. Thus, the death receptors and the Bcl-2 family represent separate molecular switches controlling apoptosis.

One promising new approach to cancer therapy attempts to cut off the tumour's blood supply by damaging growing blood vessels within the tumour. This year, we showed that in such therapies the BH3-only protein Bim drives destruction of tumour blood vessels, starving the tumour cells of vital nutrients (see opposite page). In separate studies, we showed that Bim and Mcl-1 are key players in drug resistance. Bim was found to enhance the effect of DNA-damaging chemotherapies in lymphomas, while pro-survival protein Mcl-1 impeded cell death after radiation damage. These discoveries have important implications for predicting the effectiveness of treatment strategies for tumours in which these proteins are switched on.

## Laboratory heads

**Professor Jerry Adams**
Division head

**Dr Philippe Bouillet**

**Professor Suzanne Cory**

**Dr Ruth Kluck**

**Associate Professor Clare Scott**

**Professor Andreas Strasser**
Division head

PhD student Mr Colin Hockings (below left)

PhD student Ms Natasha Anstee (below right) has received a scholarship from the Leukaemia Foundation for her research into the pro-survival protein Mcl-1 in acute myeloid leukaemia.


## New strategy to attack tumour-feeding blood vessels

**The growth of solid tumours, such as lung cancers, breast cancers and melanomas depends on nutrients and oxygen from the blood.**

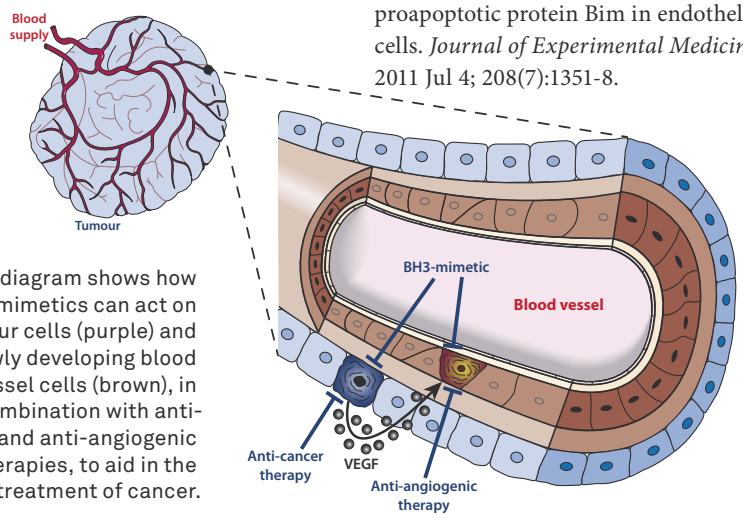
Cancer cells encourage the growth of blood vessels to feed a tumour by producing the hormone-like protein vascular endothelial growth factor (VEGF).

Scientists from the institute's Molecular Genetics of Cancer, and Cancer and Haematology divisions have discovered a key molecule needed to kill the blood vessels that supply tumours. Professor Andreas Strasser led the research, which showed that tumour-produced VEGF blocked production of Bim in the cells that line the tumour blood vessels.

The research team found that if anti-cancer therapies that target tumour blood vessels are to work, the death-inducing molecule Bim is required. The finding could lead to improved anti-cancer treatments that are based on a two- or three-pronged attack on both the tumour and its blood supply.

Professor Strasser said that strategies for treating tumours by attacking the tumour blood supply could be optimised by incorporating agents called BH3-mimetics that cause cell death by acting like Bim at a molecular level.

"A promising new approach to treating solid tumours may be to use a three-medication combination of a drug that specifically targets the tumour, an anti-angiogenic agent to impair the tumour blood vessels, and a BH3-mimetic that will help the anti-tumour drug to directly kill tumour cells and also will help the anti-angiogenic agent to starve the tumour of nutrients," Professor Strasser said.




The diagram shows how BH3-mimetics can act on tumour cells (purple) and newly developing blood vessel cells (brown), in combination with anti-cancer and anti-angiogenic therapies, to aid in the treatment of cancer.

**Funding partners:** Cancer Council Victoria, National Health and Medical Research Council, Australian Research Council, National Institutes of Health (US), The Leukemia & Lymphoma Society (US), Genentech, a member of the Roche Group, and the Victorian Government.

**More information:** Naik E, O'Reilly LA, Asselin-Labat ML, Merino D, Lin A, Cook M, Coultas L, Bouillet P, Adams JM, Strasser A. Destruction of tumor vasculature and abated tumor growth upon VEGF blockade is driven by proapoptotic protein Bim in endothelial cells. *Journal of Experimental Medicine*. 2011 Jul 4; 208(7):1351-8.

## Investing in finding leukaemia treatments

**Leukaemia is the eighth most common cancer in Australia, and more than 4800 people will be diagnosed with leukaemia this year.**

The Leukaemia Foundation has been a strong supporter of the Walter and Eliza Hall Institute's quest to find new treatments for leukaemia. The foundation has partnered with the institute to support talented young scientists for the past six years, supporting 11 institute scientists studying various aspects of blood cancer, particularly understanding how disturbances in the cell death pathway are linked to cancers.

This year, PhD student Ms Natasha Anstee received a $120,000 grant from the Leukaemia Foundation to undertake her postgraduate studies. She will study the role of pro-survival protein Mcl-1 in acute myeloid leukaemia (AML).

AMLs often express high levels of Mcl-1 and this is associated with a poor response to treatment and a poor prognosis. Ms Anstee will be testing the response of leukaemias that over-express Mcl-1 to conventional and new treatments.

"Several pharmaceutical companies are currently directing a lot of effort towards developing Mcl-1-specific drugs, with a view to improving treatment for AML and other tumours expressing high levels of Mcl-1," said Miss Anstee. "I will be comparing the efficacy of such drugs with that of existing drugs in laboratory models that have been developed at the institute."

Ms Anstee said that, despite progress being made over the past several decades in treating AML, there is a need to develop new therapies for the disease.

"AML is one of the most common forms of acute leukaemia, and despite recent advances, AML still has a poor prognosis, with only 23 per cent of patients surviving five years after diagnosis. We hope that this research will contribute to the development of new, more targeted therapies that will improve the survival rate in AML patients."

# Chemical Biology

**The Chemical Biology division focuses on developing and applying state-of-the-art chemical approaches for studying important biological and medical problems, to ultimately develop novel and improved therapeutics.**

A major research focus is cancer, particularly the role of impaired cell death in driving and maintaining tumours. One abnormality that is prominent in some types of blood cancer is overactivity of the protein Bcl-2, which acts to inhibit cell death. Our longstanding collaborations with other institute scientists have helped clarify how Bcl-2 normally functions and importantly, how it might be targeted for treating cancer. A three-way collaboration between the institute and pharmaceutical companies Genentech, a member of the Roche Group, and Abbott has led to the development of a compound called ABT-199 (GDC-0199/RG7601) that targets Bcl-2, currently in phase Ia clinical trials for patients with leukaemia.

We are continuing to investigate how cell survival is controlled, as clarifying this regulatory process may allow us to design and develop strategies to block or promote cell death. There are also active programs pursuing other cancer targets, such as key enzymes that promote tumour formation. In this regard, the division has strong links with the Cancer Therapeutics CRC.

Some of the novel therapeutic agents being investigated are also likely to be useful for diseases such as autoimmunity and inflammation. In collaboration with colleagues from the Infection and Immunity division, we are working on new treatments for malaria. An essential part of our drug discovery infrastructure is the institute's high-throughput chemical screening (HTCS) facility, which enables identification of chemical compounds that have properties suitable for their development into drugs.

Our research brings together the fundamental disciplines of chemistry and biology, and applies them to identifying, characterising and targeting molecules so we can develop better treatments for diseases such as cancer and malaria.

## Laboratory heads

**Associate Professor Jonathan Baell**

**Dr Chris Burns**

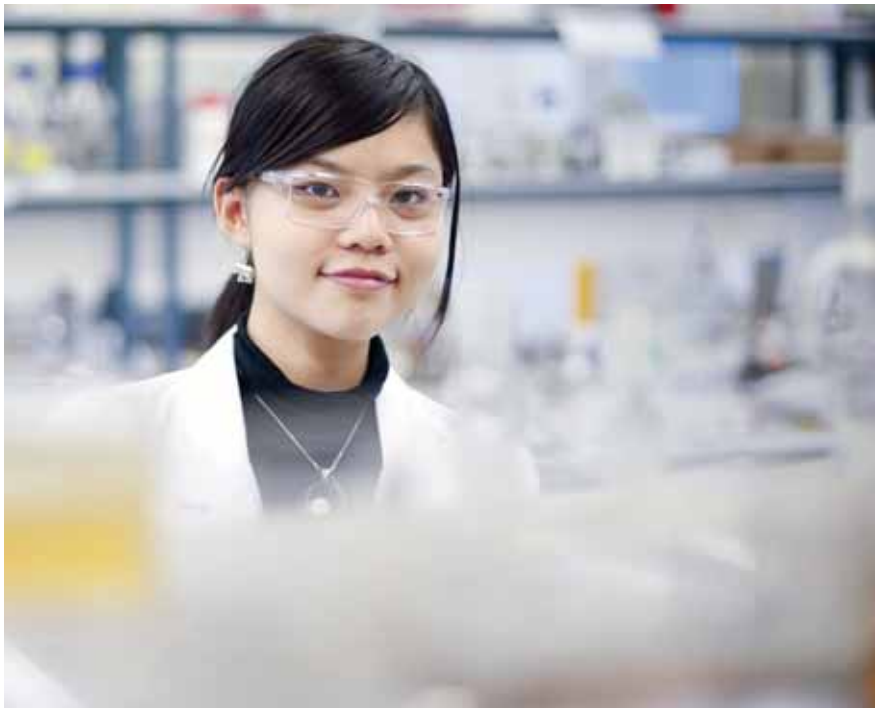
**Professor David Huang**
Division head

**Dr Guillaume Lessene**

**Dr Ian Street**

PhD student Ms Silvia Teguh (below left)

Dr Brad Sleebs (below right) is looking for ways to improve existing drugs through chemistry.



## Designing new treatments for cancer through chemistry

**Developing chemical compounds as drugs for treating disease is often a lengthy process, requiring a detailed analysis of their properties and how they interact with the body.**

Institute researchers are looking to develop new and better drugs for treating diseases such as cancers and malaria. As part of this search, they are looking for ways to improve existing drugs, such as by modifying their chemical structures to improve safety, biological activity, chemical stability or absorption by the body.

For some time, scientists from the Chemical Biology division have collaborated with industry partners Genentech, a member of the Roche group, and Abbott to develop compounds that target the Bcl-2 proteins. These proteins have been implicated in a number of cancers, including leukaemia and breast cancer.

In 2011, Dr Brad Sleebs, Associate Professor Baell and their collaborators published a paper in the *Journal of Medicinal Chemistry* in which they described creating a re-engineered compound that could kill cancer cells by binding specific Bcl-2-like proteins.

"The compound is called an 'isostere', meaning it has significantly different chemical properties to the original compound while retaining comparable biological activities," Dr Sleebs said.

"The compound we created is an isostere of an existing anti-Bcl-2 compound, replacing its central core with another. Interestingly, a detailed picture provided by our Structural Biology colleagues of how the newly created compound binds explains why its activity is subtly different from the parent compound."

Associate Professor Baell said the new agent represents the second-known class of validated Bcl-2 inhibitors.

"There is intense interest in finding new anti-cancer compounds that target Bcl-2," he said. "Our ability to manipulate them chemically enables us to improve and optimise their activity, providing us with a strong platform for developing better anti-cancer drugs."

**Collaborating organisations:** Genentech, a member of the Roche group, and Abbott.

**Funding partners:** The Leukemia & Lymphoma Society (US), National Health and Medical Research Council, Cancer Council Victoria, Australian Cancer Research Foundation, Australian Research Council and the Victorian Government.

**More information:** Sleebs BE, Czabotar PE, Fairbrother WJ, Fairlie WD, Flygare JA, Huang DC, Kersten WJ, Koehler MF, Lessene G, Lowes K, Parisot JP, Smith BJ, Smith ML, Souers AJ, Street IP, Yang H and Baell JB. Quinazoline sulfonamides as dual binders of the proteins B-cell lymphoma and B-cell lymphoma extra long with potent proapoptotic cell-based activity. *Journal of Medicinal Chemistry.* 2011 Mar 2; 54:1914.

## Chemical screening investment brings results

**A Victorian Government grant of $2.06 million in 2003 has been fundamental to the institute's role in discovering new compounds that are now entering clinical trials.**

The money, distributed through the now-defunct Science Technology Innovation (STI) scheme, funded half of the automated equipment in the institute's high-throughput chemical screening (HTCS) facility. The investment highlights the importance of taking a long-term view of research development.

The HTCS facility, located at the institute's Bundoora campus, allows the rapid screening of large chemical libraries to identify compounds that have the potential to be developed into new drugs.

Until recently, it was the only such facility at an Australian academic institution, and has been in high demand from many researchers within the institute, as well as from our academic and commercial collaborative partners.

The Chemical Biology division was established in 2010 to enhance research efforts that link biological discoveries with medicinal chemistry. This has allowed improvements in both the screening process as well as the modifications required to progress the candidate compounds into drugs.

Professor David Huang, head of the institute's Chemical Biology division, said the HTCS facility undertakes around 10 chemical screening campaigns each year.

"Discovering compounds that target cancer cells has been a major focus of our facility," Professor Huang said. "We are now seeing projects that originally started at the HTCS facility realising molecules that are entering clinical trials, which is an exciting development."

The HTCS facility has also been central to efforts to discover new treatments for infectious diseases including malaria.

"The HTCS facility has provided institute scientists with a unique opportunity to take their research a step closer to our ultimate goal of improving human health," said Professor Huang. "The Victorian Government's initial investment in the facility has already led to some potentially exciting new medications, and has enabled us to attract biotech collaborations to the state."

Ms Rebecca Moss at the high-throughput chemical screening facility.

# Molecular Medicine

**The Molecular Medicine division investigates the pathways that control the normal production of blood cells and how these pathways are perturbed in blood cell diseases such as leukaemia and lymphoma.**

We use data from genetics, genomics, proteomics and computational analyses to identify individual genes involved in regulatory pathways, with the ultimate goal of working closely with clinicians and the private sector to translate our discoveries into improvements in the diagnosis and treatment of blood diseases.

Major research themes in the division include blood cell production and function, epigenetic regulation of gene expression and the study of blood cancers. Additional projects use the genetic technologies we have developed to better understand the regulation of neural stem cells and pathways that can lead to deafness.

Research in Professor Doug Hilton's laboratory centres around the molecular pathways regulating normal blood cell production. Mature blood cells are generated by a population of stem cells which are also capable of self-renewal. Traditionally, mature blood cells and blood stem cells were thought to exist as two separate populations, with little communication. In a project spear-headed by Dr Carolyn de Graaf, we showed that mature blood cells can communicate back to their stem cell 'parents', changing the stem cells' gene expression and influencing their behaviour. Using new-generation genomic technologies the team also defined gene signatures underlying defective signalling in blood stem cells. This information could be used to diagnose and treat blood diseases in the future.

Dr Samir Taoudi, the division's newest laboratory head, is focusing on how an embryo produces the earliest stem cells. He recently showed that a gene which is frequently hijacked by prostate cancer cells, *Erg*, plays a central role in maintaining blood stem cell numbers during embryonic development and ensuring adequate stem cells exist to fully equip the adult in later life (see opposite page). This study emphasised the crucial role that *Erg* plays in maintaining healthy stem cells in times of stress.

## Laboratory heads

**Dr Marnie Blewitt**

**Dr Ross Dickins**

**Professor Doug Hilton**
Division head

**Dr Samir Taoudi**

**Dr Tim Thomas**

**Dr Anne Voss**

PhD student Ms Farrah El-Saafin (below left)

Dr Samir Taoudi (below right) has shown how the gene *Erg* plays a central role in blood stem cell maintenance.

## *Erg* gene key to blood stem cell 'self-renewal'

**Blood stem cells produce and maintain the blood system throughout an organism's lifetime. They are multipotent cells, meaning they are able to form any cell of the blood, and they self-renew, so they are a source of endless supply.**

One major barrier to their therapeutic use is that stem cells can only be isolated in numbers too low for practical use. Efforts to expand their number often cause them to turn into more mature cells.

Dr Samir Taoudi, Professor Doug Hilton and colleagues have begun to unravel how blood stem cells regenerate themselves, identifying a key gene required for the process.

The discovery that the *Erg* gene is vitally important to blood stem cells' unique ability to self-renew could give scientists new opportunities to use blood stem cells for tissue repair, transplantation and other therapeutic applications. Dr Taoudi said the research aimed to understand how blood stem cells are made.

"One of the key features of blood stem cells, one that could be exploited for therapeutic use, is their ability to regenerate or renew themselves. However, relatively little is known about how this occurs, or the molecular pathways that specifically control regeneration," he said.

The team found that during development, *Erg* was not needed for the original blood stem cells to be made, or to produce mature blood cells. "But without *Erg*, these new blood stem cells rapidly decreased as they divided to produce more blood, so that they were almost completely exhausted by the time the mouse was born," he said.

The practical aim of the research is to aid in the development of stem cell therapies, Dr Taoudi said.

"At the moment, if you take stem cells from a person and try to expand them, many of the stem cells lose their ability to regenerate. We are trying to find ways in which you could take stem cells collected from bone marrow or cord blood and 'switch on' expression of particular sets of genes, encouraging the stem cells to expand, essentially creating your own endless supply of blood stem cells," he said.

**Funding partners:** National Health and Medical Research Council, Australian Cancer Research Foundation, Australian Stem Cell Centre, Australian Research Council, The Sylvia and Charles Viertel Charitable Foundation and the Victorian Government.

**More information:** Taoudi S, Bee T, Hilton A, Knezevic K, Scott J, Willson TA, Collin C, Thomas T, Voss AK, Kile BT, Alexander WS, Pimanda JE, Hilton DJ. ERG dependence distinguishes developmental control of hematopoietic stem cell maintenance from hematopoietic specification. *Genes & Development*. 2011 Feb 1; 25(3):251-62.

## 'Hairpin' research hope for blood cancers

**Leukaemia is a cancer of the blood cells and is the eighth most common type of cancer in Australia.**

Dr Ross Dickins, a laboratory head in the Molecular Medicine division, is investigating the genes involved in leukaemia development to better understand the genetic changes that bring about leukaemia. He uses short 'hairpin' RNA (shRNA) techniques that he developed in his laboratory to help identify the function of genes by switching genes on and off to discover their function.

"The techniques harness a natural process of gene silencing known as RNA interference and allow us to quickly and effectively study multiple cancer genes in new ways," Dr Dickins said. "We are examining several genes that are known to be altered in human leukaemia, along with a new set of genes that are thought to be involved but whose functions in normal blood cells and leukaemia cells remain untested."

In 2010, Dr Dickins' research was boosted by a $1 million Viertel Fellowship. The fellowship is awarded by The Sylvia and Charles Viertel Charitable Foundation, one of the largest charitable foundations in Australia.

Dr Dickins said it was an honour to be named the 2010 Viertel Fellow. "Charles Viertel was a hugely generous Australian philanthropist, yet during his lifetime he sought little public recognition. It is a great privilege to receive a fellowship from the charitable foundation he established," he said.

Dr Dickins said the fellowship would support research to identify new therapeutic targets for cancer. "Ultimately, we hope that shRNA technology will accelerate cancer drug discovery by identifying genes that could be targeted by new therapeutic agents, in particular for leukaemias and lymphomas, and help match the genetic profile of a tumour with the best possible therapeutic agent to treat that tumour," Dr Dickins said.

Dr Ross Dickins was awarded a Viertel Fellowship to further his research into the genes responsible for leukaemias.

# Structural Biology

**Our research contributes to the discovery of new medicines through studies of the three-dimensional structures of large biological molecules that are either targets for drugs or potential therapeutic agents in their own right.**

The division's focus on apoptosis, or programmed cell death, is motivated by the belief that the Bcl-2 protein family, which controls apoptosis, is an important target for anti-cancer drugs.

The highest impact work from the division this year was from Dr Doug Fairlie's laboratory. His discovery of a mammalian-like cell death pathway in schistosomes (see opposite page) could open up new avenues for treatment of the deadly parasitic disease schistosomiasis, which is a significant health problem in developing countries.

This year, research in our division also revealed how complexes form between the pro-apoptotic protein Bax and pro-survival proteins Bcl-xL and Mcl-1. Using crystal structures of the molecules we showed that formation of the complexes requires a significant conformational change in Bax. This could have implications for drug targeting and development.

Our researchers also look at viral proteins that block the intrinsic cell death pathway by mimicking Bcl-2 proteins in order to prevent the immune system from killing virus-infected cells. We found, contrary to expectations, that the Epstein-Barr virus (EBV) protein BHRF1 binds pro-apoptotic BH3-only proteins in the same manner as Bcl-2 does, making BHRF1 a potential drug target for treating EBV.

Late in 2010 we welcomed new faculty members Drs Matthew and Melissa Call from Harvard University. In July 2011 Dr Brian Smith departed to a faculty position at La Trobe University and we look forward to continuing to collaborate with him. Dr Tom Garrett retired during the year after a career of landmark discoveries on the structure and function of cell surface receptors.

## Laboratory heads

**Dr Jeff Babon**

**Dr Matthew Call**

**Dr Melissa Call**

**Professor Peter Colman**
Division head

**Dr Doug Fairlie**

**Dr Tom Garrett**

**Dr Jacqueline Gulbis**

**Associate Professor Mike Lawrence**

**Dr Brian Smith**

**Dr Colin Ward**

Dr Erinna Lee (below left) and Dr Doug Fairlie have identified a programmed cell death pathway in parasitic worms.

## Worm 'cell death' discovery could lead to new drugs for deadly parasite

**Schistosomiasis is a deadly parasitic disease of the developing world, which ranks with malaria and tuberculosis as a major source of human illness. More than 200 million people are currently affected by the disease, and an estimated 200,000 people die from it each year.**

Dr Erinna Lee and Dr Doug Fairlie study programmed cell death in human cells, and have recently started studying the process in schistosomes, the parasitic fluke worms that cause schistosomiasis.

Dr Fairlie said that the group has shown that the cell death machinery that exists in fluke worms is unexpectedly similar to the cell death pathway in human cells.

"We found that schistosomes have a complex cell death mechanism that relies on a delicate balancing act of pro-survival and pro-death molecules, just like in humans," Dr Fairlie said. "We also determined that the three-dimensional structure of a key schistosome cell death molecule was very similar to the protein that controls the process in humans, which could potentially guide future efforts to design therapeutic agents."

Dr Lee said the team is currently exploring the possibility that so-called 'BH3-mimetic' agents could be used for treating schistosomiasis. BH3-mimetics target the cell death pathway in humans and are currently being trialled as anti-cancer treatments.

"We have found that a BH3-mimetic compound called ABT-737 binds to at least one schistosome pro-survival protein, suggesting it is feasible that BH3-like molecules could also be developed for treating schistosomiasis, and potentially other parasitic worm infections," she said.

Although the discovery could lead to exciting new possibilities for the treatment of parasitic worm diseases, Dr Fairlie said there was still a lot to be understood about the cell death process in fluke worms before this became a reality.

**Funding partners:** National Health and Medical Research Council, Australian Cancer Research Foundation, The Leukemia & Lymphoma Society (US), Leukaemia Foundation of Australia, ANZ Trustees, The CASS Foundation Limited and the Victorian Government.

**More information:** Lee EF, Clarke OB, Evangelista M, Feng Z, Speed TP, Tchoubrieva EB, Strasser A, Kalinna BH, Colman PM and Fairlie WD. Discovery and molecular characterization of a Bcl-2–regulated cell death pathway in schistosomes. *Proceedings of the National Academy of Sciences USA*. 2011 Apr 26; 108(17):6999-7003.

## Improving insulin for treating diabetes

**Type 1 diabetes is a lifelong disease that affects more than 122,000 people in Australia and is increasing at a rate of 3.2 per cent per year.**

Insulin is used successfully to manage type 1 diabetes, however it requires daily injections and comes with other potentially fatal side effects, such as low blood sugar (hypoglycaemia). Associate Professor Mike Lawrence from the institute's Structural Biology division is researching the way insulin interacts with cell surface receptors with the long-term goal of devising new treatments for diabetes.

"To enable the development of new and improved therapeutic alternatives for treating diabetes, it is essential to understand how insulin binds to the insulin receptor," Associate Professor Lawrence said.

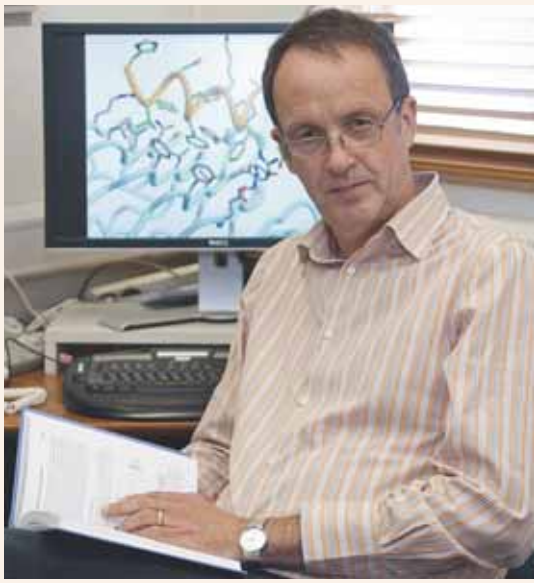
"Through this work, we hope to be able to define the binding sites of insulin on the insulin receptor and details of the binding interactions, which will give us a better understanding of how the insulin receptor functions."

In 2010, Associate Professor Lawrence received a $60,000 grant from the Diabetes Australia Research Trust (DART) to fund his studies, which use electron microscopy to study how insulin binds to the insulin receptor on the surface of cells.

Established by Diabetes Australia in 1987, DART supports and develops the field of diabetes research in Australia by providing funding towards the prevention, management and cure for diabetes.

Associate Professor Lawrence is using cryo-electron microscopy to determine the structure of the insulin–receptor complex, which allows the structure to be viewed in a state that is as close as possible to that which exists in the body. He said it might be possible to use this information for the design of new therapies, which could act like insulin with improved pharmaceutical properties.

"We would hope that, in the future, we could potentially see therapeutics available for treating diabetes which mimic insulin but offer better glycaemic control," Associate Professor Lawrence said.



Associate Professor Mike Lawrence

# Bioinformatics

**The past year has seen an enormous growth in the Bioinformatics division's efforts in the analysis of massively parallel DNA sequencing (MPS) data. What was a strong trend a year ago has grown to a near-universal preoccupation at present, as more and more colleagues embrace this rapidly developing and exciting technology.**

MPS is a type of ultra-high-throughput sequencing which is approximately 100 times faster than the previous gold standard technologies. Our efforts in this area include consulting on the design and analysis of future MPS studies, collaborating on the analysis of MPS data from projects around the world, and developing novel analytical techniques and software.

Professor Gordon Smyth and his laboratory have continued the development of new MPS analysis methods, including a software package called edgeR. Dr Tony Papenfuss has been analysing MPS data in a variety of collaborative projects, including studies of Tasmanian devil facial tumour disease and genomic rearrangements of human tumours. He has also been looking at immune gene expression in the Australian flying fox, which is the natural host of Hendra virus and Australian bat lyssavirus.

Dr Melanie Bahlo and her team have been using MPS data to map genes predisposing to disease. Professor Terry Speed has been working with collaborators at the University of California, Berkeley, on identifying binding sites of transcription factors, and studying biases in MPS data.

In addition to the explosion of new MPS data, the division has been continuing with more traditional bioinformatics research. Ms Katherine Smith and Dr Melanie Bahlo identified the gene responsible for the rare but fatal Kufs disease (see opposite page). With Dr Di Wu, Professor Smyth has published a novel statistical test that assesses the behaviour of larger biological processes instead of individual genes. Dr Papenfuss has had success in discovering gene families in mammals, including the genes which produce venom in the platypus, while Professor Speed has continued his studies of oestrogen biology with collaborators in the United States.

### Laboratory heads

**Dr Melanie Bahlo**

**Dr Tony Papenfuss**

**Professor Gordon Smyth**

**Professor Terry Speed**
Division head

Dr Melanie Bahlo (below right) and PhD student Ms Katherine Smith used innovative approaches to identify the gene responsible for Kufs disease, a rare but fatal hereditary brain disorder.

## New technology finds gene responsible for Kufs disease

**Kufs disease is a rare but fatal hereditary neurodegenerative disease, affecting approximately one in one million people.**

Brain symptoms result from a build up of fat in brain cells that is toxic to the cells, causing symptoms including epilepsy, dementia, impaired motor function and intellectual deterioration.

Dr Melanie Bahlo and colleagues from the institute's Bioinformatics division, with neurologist Professor Sam Berkovic from The University of Melbourne, have used innovative new technologies to identify that mutations in the *CLN6* gene are the cause of inherited recessive Kufs type A disease.

Professor Berkovic said identification of the *CLN6* gene would enable more efficient and much less invasive techniques for earlier diagnosis of Kufs disease. "Currently, the only way that we can diagnose this disease is to do an invasive and dangerous brain biopsy," Professor Berkovic said. "This discovery will enable us to use a rapid and simple blood test to genetically test for the disease."

Dr Bahlo's innovative work used data generated from a person's DNA, called SNP genotyping. When combined with sophisticated mathematical and statistical analyses, the information helped identify the region in the human genome likely to contain the DNA error that causes Kufs disease.

"The genetic cause of Kufs disease has remained a mystery for over 25 years, because the rarity of the condition meant that our patient groups were so small we couldn't reliably pinpoint any particular genetic mutations that caused their disease," Dr Bahlo said. "Discovering the *CLN6* gene as the cause of Kufs disease is a great outcome for us and for the people who are affected by this awful disease."

Dr Bahlo said the approach used to find the gene responsible for Kufs disease could hold the key for finding the genetic cause of a number of other hereditary diseases including other epilepsy-related diseases, deafness and some familial cancers.

**Collaborating organisations:** The University of Melbourne, C. Besta Neurological Institute, McGill University, Université de Montréal, Liverpool Hospital, University of Catania, Beaumont Hospital, University Magna Græcia, University of Modena and Reggio Emilia, University College London.

**Funding partners:** National Health and Medical Research Council, Battens Disease Support & Research Association and the Victorian Government.

**More information:** Arsov T, Smith KR, Damiano J, Franceschetti S, Canafoglia L, Bromhead CJ, Andermann E, Vears DF, Cossette P, Rajagopalan S, McDougall A, Sofia V, Farrell M, Aguglia U, Zini A, Meletti S, Morbin M, Mullen S, Andermann F, Mole SE, Bahlo M, Berkovic SF. Kufs disease, the major adult form of neuronal ceroid lipofuscinosis, caused by mutations in CLN6. *American Journal of Human Genetics*. 2011 May 13; 88(5):566-73.

## Sir John Monash scholarship to fund Oxford PhD studies

**Bioinformatician Mr Davis McCarthy has been awarded a $150,000 scholarship from the General Sir John Monash Foundation that has made it possible for him to start his PhD at the University of Oxford, UK, in 2011.**

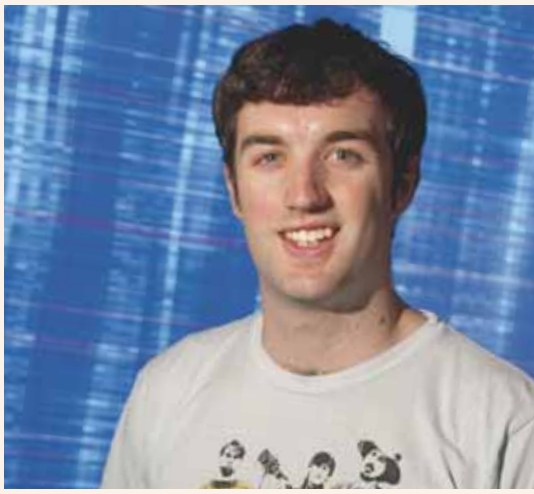
As an undergraduate and honours student in the Bioinformatics division, Mr McCarthy was a key member of the edgeR project (see opposite page). He will undertake his PhD in the Department of Statistics at Oxford, home to several leading researchers in the field who actively collaborate with the institute bioinformaticians.

"The work I propose for my PhD will help biologists to develop treatments for diseases such as cancer, malaria, and diabetes," Mr McCarthy said. "Statisticians may operate behind the scenes in improving human health, but our contributions can be wide-ranging and profound."

Recent advances in biology have been driven by the development of ultra-high-throughput DNA sequencing technologies that allow biologists to investigate the differences in thousands of genes at once. The outcome of this is the generation of an overwhelming amount of data.

"Making sense of this deluge of data presents a real challenge," Mr McCarthy said. "Statisticians aim to help biologists obtain as much useful information from their data as possible by providing robust statistical analysis techniques implemented in easy-to-use, well-documented, public software."

Mr McCarthy said there are many possible applications. "We can, for example, investigate which genes are 'differentially expressed' between tumour cells and healthy cells as a step towards understanding the mechanisms by which cancer evades the body's defence system," he said.



Mr Davis McCarthy

# Infection and Immunity

**Infectious diseases caused by parasites, bacteria and viruses are a major global health burden resulting in death, disability, and social and economic disruption for hundreds of millions of people.**

Malaria, tuberculosis and HIV are three infectious diseases that cause significant death and disability, particularly in resource-poor countries.

In the Infection and Immunity division we aim to understand how infectious agents cause disease in humans and to use this knowledge to develop new treatments. A highlight of the division this year has been our work on understanding the factors that impede immune responses to persistent virus infections such as HIV. A team led by Dr Marc Pellegrini identified that the cell signalling protein interleukin-7 is a potential therapeutic agent for the treatment of chronic viral diseases such as HIV (see opposite page). The discovery, using a mouse model infected with the virus LCMV (lymphocytic choriomeningitis virus), has enabled an understanding of the inhibitory pathways underlying impaired antiviral immune responses.

The division continues to make discoveries and advances in the understanding of malaria. The malaria-causing *Plasmodium* parasite infects humans by invading red blood cells, where it can access the nutrients it requires for survival. An important aim of the division has been to understand how the parasite infects a red blood cell. The advent of super-resolution microscopy has allowed us to visualise and dissect the steps in this host-cell invasion process. The ability to break down each molecular step has enabled us to build a comprehensive model for the molecular basis of parasite invasion.

We have made further inroads into understanding this invasion process by identifying complement receptor-1 on the red blood cell as a major receptor to which the malaria parasite binds using the protein PfRh4. This allows the parasite to identify the appropriate cell to enter, resulting in activation of the multiple steps in the invasion process.

## Laboratory heads

**Dr Alyssa Barry**

**Dr Jacob Baum**

**Dr James Beeson**

**Professor Alan Cowman**
Division head

**Dr Diana Hansen**

**Professor Ivo Mueller**

**Dr Marc Pellegrini**

**Associate Professor Louis Schofield**

**Dr Chris Tonkin**

Dr Jake Baum (below left) and PhD student Mr David Riglar

Dr Alyssa Barry (below right)

## Boosting immune response may hold key to HIV cure

**Viruses such as HIV and hepatitis B and C often lead to the establishment of incurable, lifelong infections due to the immune system's inability to effectively respond to and clear the virus.**

Despite tremendous efforts from the immune system, particularly T cells, these viruses are able to establish chronic infections by overwhelming the immune system to the point where it is overrun and effectively 'gives up' on fighting the infection.

However, in a 2011 *Cell* paper, Dr Marc Pellegrini and colleagues Mr Jesse Toe and Mr Simon Preston showed that they were able to successfully clear an HIV-like infection in mice by reinvigorating T cell responses to the virus.

Dr Pellegrini said treatment with a cell signalling protein called interleukin-7 (IL-7) boosted the immune response to virus infection, allowing the mice to completely clear the virus. "We found that IL-7 boosted the immune response in a profound fashion, such that animals were able to gradually clear the virus without too much collateral tissue damage," he said.

Further investigations revealed that, at the molecular level, IL-7 worked by switching off a gene called *SOCS3* in T cells. "In an overwhelming infection such as HIV and hepatitis B and C, *SOCS3* becomes highly activated and suppresses the immune response, probably as a natural precaution to prevent tissue damage. IL-7 treatment during a viral infection switches *SOCS3* off, boosting T cell numbers and function so that the immune system can successfully fight the virus until it is cleared," Dr Pellegrini said.

The finding could lead to a cure for HIV, hepatitis B and C, and bacterial infections such as tuberculosis, which are significant economic and global health burdens.

**Collaborating organisations:** Ontario Cancer Institute, Cytheris Inc, Stanford University, TWINCORE – Centre for Experimental and Clinical Infection Research, Duke University, Harvard University, Queen's University.

**Funding partners:** National Health and Medical Research Council, Canadian Institute for Health, Cancer Research Institute and the Victorian Government.

**More information:** Pellegrini M, Calzascia T, Toe JG, Preston SP, Lin AE, Elford AR, Shahinian A, Lang PA, Lang KS, Morre M, Assouline B, Lahl K, Sparwasser T, Tedder TF, Paik J, DePinho RA, Basta S, Ohashi PS, Mak TW. IL-7 engages multiple mechanisms to overcome chronic viral infection and limit organ pathology. *Cell*. 2011 Feb 18; 144:1-13.

A collage showing progressive clearance of virus (green) due to treatment with IL-7. T cells (white/brown) are superimposed on the virus-infected cells, with a 'halo' of IL-7 boosting their ability to fight and eliminate virus.

## Unravelling the secrets of malaria

**Malaria is a devastating parasitic infection. Every year, *Plasmodium* parasites infect more than 600 million people worldwide, resulting in almost one million deaths, mostly children.**

Resistance to common antimalarial drugs is now widespread, highlighting an urgent need for new therapies.

In 2010, institute researcher Dr Justin Boddey was awarded a Ramaciotti Establishment Grant of $75,000 to continue his research on whether the mechanism used by malaria parasites to renovate red blood cells is also used in the liver infection stage.

Dr Boddey said his Ramaciotti grant would help to answer basic, fundamental questions about how malaria infects cells.

"We are interested in looking at the early stages of human infection, where, for about a week, the parasite uses the liver as a safe-haven to mount an attack on red blood cells," he said.

The Ramaciotti Foundations, administered through Perpetual, have been a strong supporter of the Walter and Eliza Hall Institute since 1971. The general manager of philanthropy at Perpetual, Mr Andrew Thomas, said Vera Ramaciotti was a forward-thinking philanthropist.

"Vera made a significant and lasting contribution to the Australian scientific community through her decision to create a charitable trust 40 years ago," he said. "Since then, the Ramaciotti Foundations have provided scientists with necessary funds for creative and cutting-edge medical research, which often struggles to attract funding from mainstream sources."

The Ramaciotti Foundations have donated more than $51 million to biomedical research in Australia and are collectively one of the largest private contributors to the field.

# Immunology

**Our immune system is capable of tremendous information gathering and processing; probing and responding to features of foreign material. For the immune system, decisions on how to respond to foreign or diseased cells and pathogens begin at birth and continue throughout life.**

In the Immunology division, our laboratories are dedicated to understanding the fascinating but complex immune system, both in its healthy state and when its processes go awry. We are motivated by the knowledge that developing accurate models of the adaptive immune response, which recreate these decision-making and control responses, will have enormous practical benefits for human health.

Our scientists are working on these problems at multiple levels. We carefully dissect the behaviour of lymphocytes (a type of white blood cell) and their interactions with other cells to define the molecular components and rules governing lymphocyte function. This information is being used to derive working computer models that accurately simulate the immune response.

Other studies examine the regulation of immune cell function to determine the genetic basis of particular responses, and how these responses might be manipulated for therapeutic benefit. We are particularly interested in understanding how antibody production is controlled, with a view to improving vaccination strategies.

A major area of discovery has been the development of ways to switch off the immune response. These methods are finding application in preventing tissue graft rejection and type 1 diabetes. Our studies have led to a new strategy to identify people with a susceptibility to developing type 1 diabetes, and to modify these people's immune response to reduce their risk. Similar strategies are also being applied to coeliac disease, a problem caused by immune sensitivity to gluten in wheat and other foods. Members of the division are leading efforts to screen for, and eliminate, this disease.

## Laboratory heads

**Dr Bob Anderson**

**Professor Len Harrison**

**Professor Phil Hodgkin**
Division head

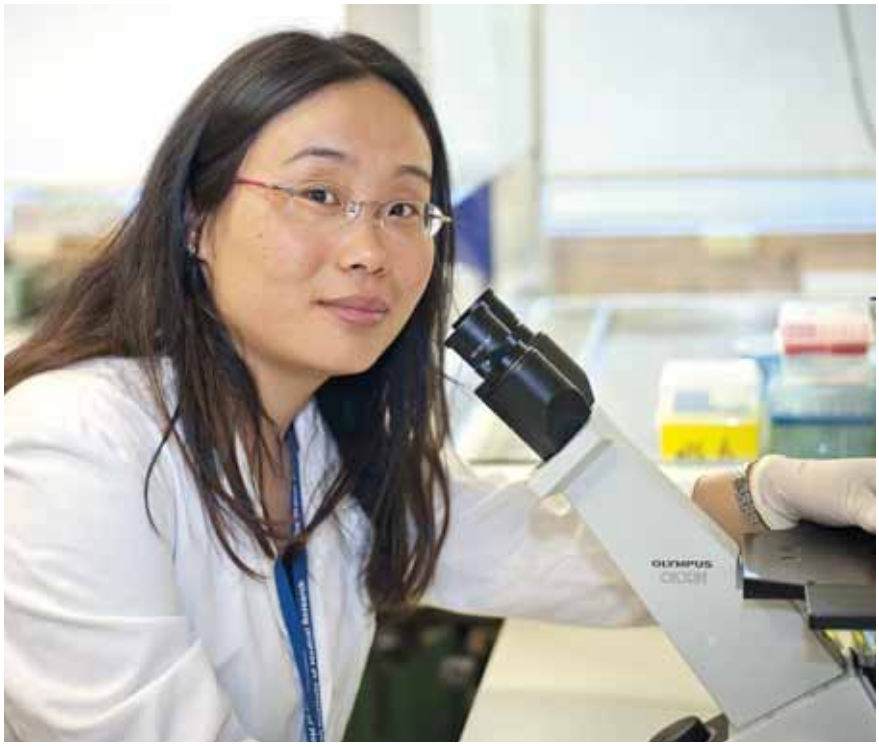
**Associate Professor Andrew Lew**

**Professor Ken Shortman**

**Associate Professor David Tarlinton**

Dr Yuxia Zhang (below left)

Hons student Ms Julia Marchingo (below right)




## Cell survival protein discovery rewrites immune system story

**B cells are a crucial component of the immune system, producing a range of antibodies that fight infection.**

One particular group of B cells, called memory B cells, are essential for the long-lived immunity that arises after immunisation. To develop into memory cells, B cells have to survive the natural process of apoptosis, or programmed cell death, that occurs following a large immune response. B cell memory is programmed in temporary cellular structures called germinal centres that develop in response to activation of the immune system.

A discovery by Dr Ingela Vikstrom and Associate Professor David Tarlinton is set to rewrite a long-held belief about how the body's immune system establishes memory B cells in these germinal centres.

Dr Vikstrom said so-called 'pro-survival' proteins regulate B cell survival and are responsible for instructing activated B cells on whether to live or die. "Our research used genetic and pharmacological methods to identify which pro-survival molecules were essential for 'instructing' these cells to establish germinal centres, as well as instructing activated B cells to become memory B cells," Dr Vikstrom said.

She said she was surprised by what they found. "We studied two well-known pro-survival proteins called Bcl-xL and Mcl-1, which we knew were involved in the process," Dr Vikstrom said. "It surprised us to find that Mcl-1 was the essential pro-survival protein required for creation and maintenance of B cell memory, not Bcl-xL as was commonly believed," Dr Vikstrom said.

Associate Professor Tarlinton said the discovery could have implications for cancer treatment, autoimmune disease and transplant rejection.

**Collaborating organisations:** Research Institute of Molecular Pathology, Vienna Biocenter.

**Funding partners:** National Health and Medical Research Council, The Leukemia & Lymphoma Society (US), National Institutes of Health (US) and the Victorian Government.

**More information:** Vikstrom I, Carotta S, Luthje K, Peperzak V, Jost PJ, Glaser S, Busslinger M, Bouillet P, Strasser A, Nutt SL and Tarlinton DM. Mcl-1 is essential for germinal centre formation and B cell memory. *Science.* 2010 Nov 19; 330:1095-1099.

Dr Ingela Vikstrom (above left) and Associate Professor David Tarlinton are researching the development of immune memory cells.

## EMBO fellowship supports blood cancer research

**Multiple myeloma is a cancer of plasma cells and is the second-most common blood cancer. It represents approximately one per cent of all cancers and two per cent of all cancer deaths worldwide.**

In 2010 Dr Victor Peperzak was awarded an EMBO (European Molecular Biology Organization) Long-Term Fellowship which allowed him to move from the Netherlands to Australia, and the institute's Immunology division, to study the molecular signals within plasma cells.

"Plasma cells are specialised in producing large amounts of antibodies and are a crucial part of our immune system," Dr Peperzak said. "Understanding how plasma cells are able to survive and continue to produce antibodies for several months up to many years is instrumental to understanding what goes wrong in these cells to cause them to become cancerous."

Dr Peperzak said plasma cells depend heavily on the continuous receipt of survival signals from the local environment for their long-term survival. His research is looking at how these external signals affect pro-survival proteins that keep the plasma cell alive.

"This project will look at whether the protein Mcl-1 is essential for maintaining plasma cells and how expression of Mcl-1 changes during development," he said. "Understanding the function and expression of Mcl-1 in plasma cells and in multiple myeloma cells might provide valuable therapeutic targets for treatment of plasma cell malignancies."

EMBO Long-Term Fellowships support postdoctoral researchers visiting laboratories throughout the world. International exchange is a key feature of the program.

Dr Victor Peperzak

# Autoimmunity and Transplantation

*This division ceased operations on 31 December 2010.*

**The immune system protects the body against disease by attacking foreign threats such as infections and tumours. In some instances, however, the immune system mistakenly targets the body's own tissues, causing autoimmune disease.**

For example, in type 1 diabetes the insulin-producing beta cells of the pancreas are targeted and damaged, and in rheumatoid arthritis the joints. In coeliac disease, the immune system damages the gut by reacting to a foreign protein, gluten, present in wheat and other cereals.

The division investigates the genetic and environmental factors leading to inflammatory diseases, as well as the underlying mechanisms, to improve disease prevention and treatment. We also investigate ways to temper immune responses to prevent rejection of transplanted tissue grafts, how inflammation in fat tissue in obese people leads to insulin resistance and diabetes, and whether stem cells in the pancreas can be used as a source of insulin-producing cells to treat type 1 diabetes.

Our research uses a broad range of molecular and cellular technologies, as well as mouse models of human diseases. Laboratory research is complemented by strong ties with clinical medicine – three of our laboratory heads hold appointments at Melbourne Health or Bayside Health, facilitating translation of research to human health.

Research highlights in the past year include: demonstrating the safety, tolerability and bioactivity of a peptide-based vaccine for coeliac disease (in collaboration with commercial biotechnology partner ImmusanT); the discovery that monocyte-derived dendritic cells are key producers of the blood cell hormone (cytokine) interleukin-12 during inflammation; demonstrating that antagonists of the pro-survival Bcl-2 family have therapeutic potential in autoimmune arthritis; evidence in human obesity that inflammatory cells in the fat tissue produce factors that block the actions of insulin; discovery of a mechanism that explains how some immune cells dampen inflammation; and demonstrating in humans that a nasal insulin vaccine desensitises the body to insulin.

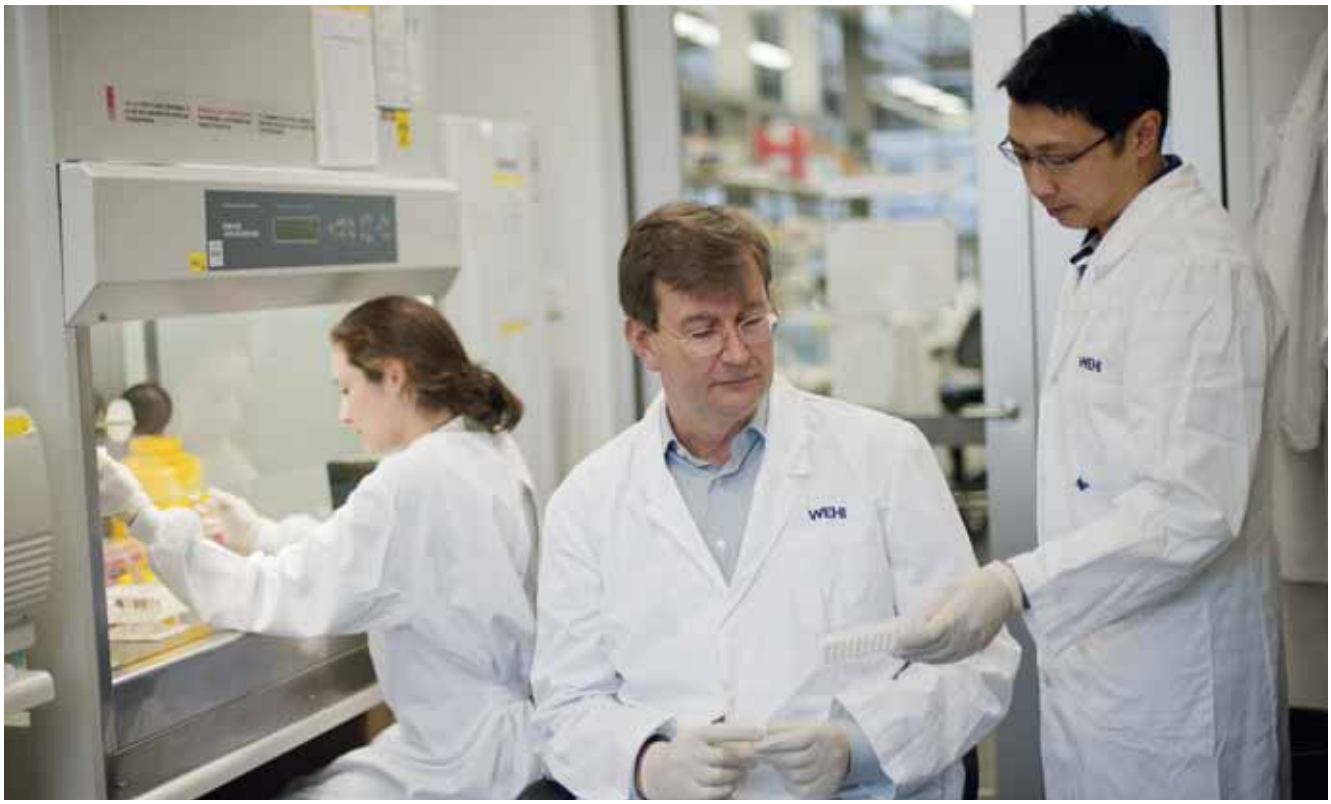
## Laboratory heads

**Dr Bob Anderson**

**Professor Len Harrison**
Division head

**Associate Professor Andrew Lew**

**Professor Ian Wicks**



Dr Melinda Hardy (below left), Dr Bob Anderson (below centre) and Dr Jason Tye-Din are trying to find new therapies for coeliac disease.

## Nasal vaccine for type 1 diabetes shows promise

**Type 1 diabetes occurs when the body's immune system attacks and kills beta cells – the cells in the pancreas that produce insulin.**

Crucially, insulin itself is a specific target of the immune attack that kills the beta cells. Lack of insulin leads to serious health problems and people with type 1 diabetes require daily insulin injections.

A nasal spray vaccine could prevent the development of type 1 diabetes in people at risk of getting the disease.

Professor Len Harrison from the institute and Professor Peter Colman and Dr Spiros Fourlanos from The Royal Melbourne Hospital have provided the first evidence in humans that the nasal insulin vaccine desensitises the human immune system, suppressing its reaction against insulin. Their research provides proof-of-principle for the type 1 diabetes prevention trial, also called the intranasal insulin trial II (INIT II), being conducted in Australia, New Zealand and Germany.

"The results showed that the vaccine allowed the immune system to restore immune tolerance to insulin, and encourages us that we are on the right track to finding a vaccine for type 1 diabetes," Professor Harrison said.

"The nasal insulin vaccine works to desensitise the immune system to insulin, which we hope will prevent a subset of white blood cells, called T cells, from attacking insulin in the beta cells of the pancreas."

**Collaborating institution:** The Royal Melbourne Hospital.

**Funding partners:** Melbourne Health, National Health and Medical Research Council, Juvenile Diabetes Research Foundation, Diabetes Vaccine Development Centre (Garvan Institute of Medical Research) and the Victorian Government.

**More information:** Fourlanos S, Perry C, Gellert SA, Martinuzzi E, Mallone R, Butler J, Colman PG, Harrison LC. Evidence that nasal insulin induces immune tolerance to insulin in adults with autoimmune diabetes. *Diabetes*. 2011 Apr; 60(4):1237-45.

## The J.H.A. Munro Foundation – supporting diabetes research

**Mr Bob Munro understands what it is like to have a family affected by serious illness.**

With a son who has severe type 1 diabetes, Mr Munro decided he wanted to make a difference to people suffering from this chronic disease, and aid in the identification of causes and treatments for diabetes. Type 1 diabetes is a lifelong inflammatory disease requiring daily injections of insulin.

For several years Mr Munro, through the J.H.A. Munro Foundation, has supported the work of Professor Len Harrison. Professor Harrison has joint appointments at the institute, where he leads the diabetes research program, and at The Royal Melbourne Hospital (RMH), where he is a member of the Department of Diabetes and Endocrinology.

Initially, Mr Munro supported the work of Professor Harrison and Professor Peter Colman (from RMH) in their development of a nasal vaccine for type 1 diabetes. This association led to Mr Munro supporting Professor Harrison's work at the institute into the role of vitamin D in diabetes. Vitamin D is a steroid hormone with anti-inflammatory properties, and has been shown to improve the function of insulin production in humans.

Professor Harrison, with fellow institute clinician researchers Dr Shirley Elkassaby and Dr John Wentworth, and Dr Spiros Fourlanos from The Royal Melbourne Hospital, has been investigating whether vitamin D improves immune and metabolic function in people with diabetes.

Mr Munro's foresight and generosity in supporting the research made the project viable.

"I wanted to put my money into research which would make a difference to people suffering from diabetes," Mr Munro said.

As results from the study became available in late 2010, the institute arranged for Mr Munro to come in for an update on the research.

"Professor Harrison and his research team and even institute director Professor Doug Hilton took the time to explain the research to me, and I felt I could be part of the solution," he said.

Mr Bob Munro, supporting diabetes research at the institute.

# Cell Signalling and Cell Death

*This division began operations in January 2011.*

**The ultimate fate of most of our cells is not to wear out or be killed, but to self-destruct in a process that has evolved specifically to maintain the correct number of cells, or remove those that are unhealthy or unwanted.**

By determining how this process occurs at a molecular level, as well as the signalling pathways that control it, we seek to find new ways of preventing the death of cells in cases where it is inappropriate, such as in neurodegenerative diseases, or restart the process when it fails, such as in some cancers or in certain autoimmune diseases.

The Cell Signalling and Cell Death division officially started in January 2011, but members of the division have had a long association with the institute. Associate Professor John Silke studies proteins called ubiquitin ligases to decipher their roles in blood cell hormone (cytokine) signalling and protein turnover, and Associate Professor Paul Ekert is focusing on leukaemias and the role of *Hox* and *Bcl2*-family genes in the development of leukaemia. Dr Grant Dewson works with Dr Ruth Kluck from the Molecular Genetics of Cancer division to investigate how Bax and Bak proteins operate, while Professor David Vaux focuses on RIP kinases, which can activate both caspase-dependent and independent cell death mechanisms in response to cytokines such as tumour necrosis factor.

A major focus of the division is understanding the mechanisms of cell death, including a family of cell death-inhibitory proteins known as IAPs. As the IAP genes are frequently amplified in cancers, we are studying how they keep tumour cells alive, as well as looking at the role of IAPs during cancer development and in healthy cells. Our identification, several years ago, of a natural IAP-antagonist led to development of IAP-antagonist compounds (also known as 'smac-mimetics'). We are studying how these compounds, which are currently in phase I clinical trials for the treatment of cancer, not only block IAP protein function, but cause IAPs to disappear from within the cell.

## Laboratory heads

**Dr Grant Dewson**

**Associate Professor Paul Ekert**

**Associate Professor John Silke**

**Professor David Vaux**
Division head

Associate Professor Paul Ekert (below left)
Dr Kate Lawlor (below right)

## Understanding how TNF controls cell signalling

**Members of the tumour necrosis factor (TNF) family of signalling molecules (cytokines) play an important role in the immune response and inflammation.**

TNF is a vital immune system protein that controls the function of immune cells, stimulates early immune responses to bacterial and viral infections, and inhibits tumour development.

Associate Professor John Silke and Dr Andrew Webb are looking at how TNF signalling molecules function and interact, which could have potential implications for treating inflammatory diseases and cancer.

Associate Professor Silke said the research, published in the journal *Nature*, described the discovery of a new gene involved in TNF signalling. "We identified for the first time that a protein called SHARPIN is involved in the signalling pathway, and interacts with two previously identified proteins, HOIL-1 and HOIP, to form a ubiquitin ligase complex," he said.

"The ubiquitin ligase complex is important for attaching ubiquitin molecules to proteins in a linear chain that 'tags' the proteins for alteration, relocation or destruction. The identification of this linear chain was very significant for the field," Associate Professor Silke said. "The number, length and linkage of these ubiquitin chains forms a language that we are just beginning to decipher."

Associate Professor Silke said the team unexpectedly found that the absence of the *Sharpin* gene induced a severe inflammatory skin disease in mouse models.

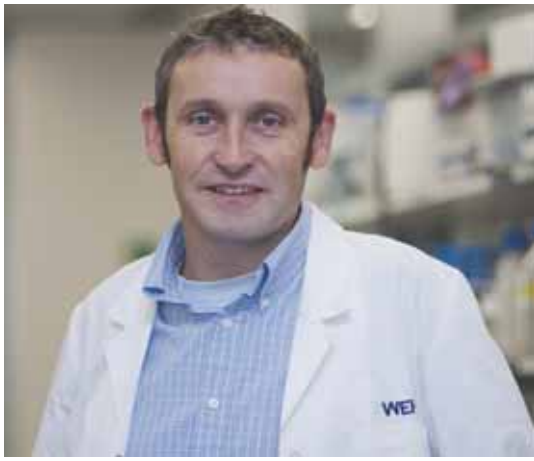
"Mice without the *Sharpin* gene had weaker TNF signalling responses, however this actually produced a strong inflammatory reaction, which was alleviated when TNF genes were switched off," Associate Professor Silke said. "This was a surprising result, because you would think that weaker TNF signals would reduce the inflammatory reaction, but it appears the body compensates for this by producing other inflammatory cytokines," he said.

**Collaborating organisations:** Imperial College London, German Cancer Research Center, Mediterranean Institute of Oncology, and Bio21 Institute.

**Funding partner:** National Health and Medical Research Council.

**More information:** Gerlach B, Cordier SM, Schmukle AC, Emmerich CH, Rieser E, Haas TL, Webb AI, Rickard JA, Anderton H, Wong WW, Nachbur U, Gangoda L, Warnken U, Purcell AW, Silke J, Walczak H. Linear ubiquitination prevents inflammation and regulates immune signalling. *Nature*. 2011 Mar 31; 471(7340):591-6.

*This work was carried out by members of the Cell Signalling and Cell Death division while the staff were at the Department of Biochemistry at La Trobe University, Melbourne.*



Associate Professor John Silke

## Remembering Philip Hemstritch (23 July 1951 – 17 March 2010)

**In 2010, when Mrs Jane Hemstritch first visited the Walter and Eliza Hall Institute, she had an intense discussion with institute director Professor Doug Hilton and head of fundraising Ms Deb Cutts about the institute's research aspirations.**

"I visited the cancer research laboratories and had a great discussion with Doug and Deb about the institute's cancer research, which aimed to explore the behaviour of cancer in order to develop innovative new treatments," Mrs Hemstritch said. "I was eager to help support the institute in any way I could to see them achieve this mission."

With a background in accounting and science, Mrs Hemstritch was asked to join the institute's Financial Sustainability Committee in April 2011 to help raise funds to support the sort of critical clinical research that will improve the lives of people with all types of cancer.

She also decided to make a significant donation to cancer research in honour of her husband Philip who died in 2010 after a two-and-a-half year battle with pancreatic cancer. "I looked into the research that the institute was doing to better understand cancers that arise from mutations that help tumour cells to survive," Mrs Hemstritch said.

In looking at the research streams she could support, Mrs Hemstritch settled on the work undertaken by the institute's Cell Signalling and Cell Death division, led by Professor David Vaux. Professor Vaux's work focuses on apoptosis, or programmed cell death.

A discovery Professor Vaux made 20 years ago has led to the development of a potential new anti-cancer agent that is now entering clinical trials to treat chronic lymphocytic leukaemia, the most common type of leukaemia. Mrs Hemstritch's support of his division will assist in this research.

# Inflammation

*This division began operations in January 2011.*

**Inflammation is a rapid, protective response to noxious stimuli. A wide variety of stimuli can induce inflammation and an intricate system of recognition receptors, immune cells and mediators coordinate and control the response in affected tissues and the body.**

Short-term inflammation is usually beneficial to the host, but can be catastrophic if not controlled appropriately. Increasing evidence suggests persistent, low-grade inflammation is likely to contribute to many common diseases, including autoimmune and metabolic conditions, and cancer.

In the Inflammation division we study the biological and molecular mechanisms underlying inflammatory diseases in order to improve prevention and treatment. We are interested in acute and chronic infections, autoimmune diseases (such as rheumatoid arthritis, vasculitis and rheumatic fever) and metabolic diseases (such as atherosclerosis and gout). We study cell signalling proteins (cytokines), immune cells and molecular regulators of inflammation using a wide range of experimental techniques. We have strong connections to hospitals, facilitating translation of research to human health.

Research highlights from the division in its first six months include describing how a cytokine discovered at the institute, granulocyte-macrophage colony stimulating factor (GM-CSF), coordinates the recruitment and differentiation of a type of dendritic cell that promotes ongoing inflammation. Recent studies of the iNOS enzyme, which catalyses the production of nitric oxide to kill pathogens, have demonstrated that a molecule known as SPSB1 regulates iNOS during the early response to pathogens.

Our division has also developed an automated high-throughput live cell-imaging platform to examine cell survival. We have demonstrated that the Bcl-2 family of cell death proteins can directly regulate the Fas death receptor pathway in neutrophils, highlighting novel avenues to control apoptosis during inflammatory disease.

Currently under study are the molecular mechanisms underlying the regulation of cystatin C, a protein that has been linked to atherosclerosis and is regulated by inflammatory stimuli through expression of the transcription factor IRF8. This may lead to development of therapeutic treatments to prevent atherosclerosis.

## Laboratory heads

**Dr Ben Croker**

**Dr Sandra Nicholson**

**Dr José Villadangos**

**Professor Ian Wicks**
Division head

Dr Sandra Nicholson (below left)

PhD student Dr Simon Chatfield (below right)

## Defining the molecular 'conversations' leading to inflammatory disease

**Chronic inflammatory diseases such as rheumatoid arthritis are a major health burden in Australia.**

Dr Ian Campbell, Ms Annemarie van Nieuwenhuijze and Professor Ian Wicks in the Inflammation division have discovered a biological sequence of events that leads to the development of inflammatory disease.

The studies build on longstanding research headed by Professor Wicks, which has explored the roles of the molecules (cytokines) G-CSF (granulocyte colony stimulating factor) and GM-CSF (granulocyte-macrophage colony stimulating factor) in mediating the joint inflammation that causes arthritis.

"The role of G-CSF and GM-CSF in blood cell formation have been well defined by a large body of research by institute scientists, in particular Professor Don Metcalf," said Professor Wicks.

"Understanding how these cytokines can be manipulated to treat chronic inflammatory diseases is an exciting field which is already leading to new agents entering clinical trials."

The current study has shown that a subset of immune cells called 'helper T cells' produces GM-CSF, which drives the formation of other immune cells, called inflammatory dendritic cells, that exacerbate joint inflammation. This work was facilitated by collaboration with the dendritic cell group, headed by Dr José Villadangos. Treatments that stop this molecular communication between the T cells and the inflammatory dendritic cells may be able to reduce the inflammation that causes rheumatoid arthritis, said Professor Wicks.

"Currently, around half of patients do not respond adequately to available therapies for arthritis," he said. "As a rheumatologist, I am very excited that our research could have opened a whole new field of treatment to help these patients. We are also hopeful that inhibitors of GM-CSF signalling might have fewer, and more manageable, side effects than current treatments."

**Funding partners:** John T Reid Charitable Trusts, Arthritis Foundation of Australia, National Health and Medical Research Council, Cancer Council Victoria, European Commission and the Victorian Government.

**More information:** Campbell IK, van Nieuwenhuijze A, Segura E, O'Donnell K, Coghill E, Hommel M, Gerondakis S, Villadangos JA, Wicks IP. Differentiation of inflammatory dendritic cells is mediated by NF-κB1-dependent GM-CSF production in CD4 T cells. *Journal of Immunology*. 2011 May 1; 186(9):5468-77.

## Arthritis research program flourishes under long-term support

**Rheumatoid arthritis is a major cause of disability and chronic pain for around 200,000 Australians. It is estimated to cost the community billions of dollars per year in direct and indirect medical care, lost earnings and productivity.**

The institute has been fortunate to have the long-term support of the John T Reid Charitable Trusts in maintaining an arthritis research laboratory. The Reid Laboratory has been headed by Professor Ian Wicks since the early 1990s, and is now part of the newly formed Inflammation division.

The Reid Laboratory has made many substantial advances in understanding the molecular events underlying the development of arthritis. One highlight has been the discovery that the cytokines G-CSF and GM-CSF contribute to the joint inflammation that underlies arthritis. This research has resulted in the development of potential new treatments for arthritis that block G-CSF or GM-CSF, the latter now being in phase I clinical trials.

"G-CSF and GM-CSF were both discovered at the institute as regulators of white blood cell production," said Professor Wicks. "Our work has opened a new avenue of interest into the role of these cytokines in inflammation, which we hope will lead to new treatments for inflammation and arthritis.

"Research into the causes of, and treatments for rheumatoid arthritis remains relatively poorly supported in Australia, despite the significant impact this disease has on the community," Professor Wicks said. "The support of the John T Reid Charitable Trusts has provided my laboratory with a critical support base from which we can develop long-term research strategies that span from basic discovery through to clinical research."

Mrs Belinda Lawson (centre), trustee of the John T Reid Charitable Trusts, with institute researchers including director Professor Doug Hilton (far left) and Professor Ian Wicks (third from left).

# Molecular Immunology

*This division began operations in January 2011.*

**Our health depends on a complex network of immune cells that perform the delicate balancing act of protecting us from attack by invading microorganisms whilst limiting the collateral damage to the body's own cells.**

The Molecular Immunology division was created in January 2011 with the goal of deciphering how our immune network functions and what goes awry in conditions such as autoimmune disease and leukaemia.

All cells in the immune system derive from blood stem cells that reside in the bone marrow. Major research themes of the division are to investigate how these rare stem cells generate immune system cells and how the mature components of the system such as B cells, T cells, natural killer cells and dendritic cells are programmed to undertake their specialised functions.

This year we have made a number of discoveries that have improved our understanding of how this immune cell programming occurs. In a project led by Dr Gabrielle Belz we discovered that the presence of inhibitory factor Id2 is critical for the decision of immature cells to become either dendritic cells, sentinels that alert the immune system to foreign invaders, or natural killer cells, which eliminate virus-infected and cancerous cells (see opposite page).

Another project of long-term interest is understanding the master immune regulator Blimp-1. Mice lacking Blimp-1 develop severe autoimmune disease that resembles colitis. Studies led by Drs Erika Cretney and Axel Kallies solved this mystery by finding that Blimp-1 controls the function of regulatory T cells.

Regulatory T cells provide an essential 'balance' to the system by preventing overactive immune cells attacking the body, however there are associated problems. Impaired regulatory T cell function is linked with diseases including type-1 diabetes, because the immune system isn't held in check, however too much regulatory T cell activity stops the immune system from eliminating cancer cells and impedes cancer therapy. The finding that Blimp-1 controls regulatory T cell activity opens new avenues for treating these devastating diseases.

## Laboratory heads

**Dr Gabrielle Belz**

**Dr Sebastian Carotta**

**Associate Professor Lynn Corcoran**

**Dr Axel Kallies**

**Dr Stephen Nutt**
Division head

**Dr Li Wu**

Dr Gabrielle Belz (below left) and Dr Sebastian Carotta study molecular signals in immune cells.

## Key genetic 'switch' gives clues about immune cell function

**Natural killer (NK) cells and dendritic cells (DCs) are the first line of defence in the immune response against invading pathogens and tumour development.**

There are still many holes in our understanding of the biology of NK cells and DCs, particularly their early development. Discovering how these cells progress from immature to mature immune cells will offer opportunities for exploiting them as vaccine targets or therapeutic treatments for cancer, inflammatory diseases or infection.

Researchers from the Molecular Immunology division are working to further our understanding of which genes are important for instructing blood stem cells to produce NK cells and DCs. Dr Gabrielle Belz, Dr Sebastian Carotta and colleagues have been using a key immune protein, inhibitor of DNA binding-2 (Id2), to provide insights into these elusive cells.

"Id2 is a critical protein in the immature immune cell's decision to become either a dendritic cell or a natural killer cell," Dr Belz said. "We have been using this protein to characterise these cells further, including the pathway by which they develop, what type of cell surface proteins or 'markers' they have and the genes which are important for their specific function."

Dr Carotta said that Id2 has been vital in identifying early NK progenitor populations and their development. "In collaboration with Dr Belz, we were able to use Id2 to identify and purify the earliest known population of cells which are 'committed' to becoming NK cells, which was a landmark for the field," he said.

Dr Belz said that Id2 was also helping the group map the development of different types of dendritic cells from a common ancestor, and identify other genes involved in the process.

"Our ultimate goal is to devise ways to manipulate the production of NK and dendritic cells to treat diseases such as cancer. Understanding more about the biology of these cells will uncover new ways to do this," she said.

**Funding partners:** National Health and Medical Research Council, Australian Research Council, Swiss National Science Foundation, The Sylvia and Charles Viertel Foundation, Howard Hughes Medical Institute, Leukaemia Foundation of Australia, Pfizer Australia and the Victorian Government.

**More information:** Carotta S, Pang SH, Nutt SL and Belz GT. Identification of the earliest NK cell precursor in the mouse bone marrow. *Blood*. 2011 May 19; 117(20):5449-5452.

Jackson JT, Hu Y, Liu R, Masson F, D'Amico A, Carotta S, Xin A, Camilleri MJ, Mount AM, Kallies A, Wu L, Smyth GK, Nutt SL, Belz GT. Id2 expression delineates differential checkpoints in the genetic program of CD8α(+) and CD103(+) dendritic cell lineages. *EMBO Journal*. 2011 May 17; 30(13): 2690-2704.

## Swiss investment helps immune system understanding

**Antibodies secreted by plasma cells are crucial for longlasting protection against pathogens and for efficient vaccines.**

Plasma cell development from their B cell 'parents' has to be tightly regulated to avoid severe diseases, such as autoimmunity and cancer. Plasma cell mutations lead to cancers such as multiple myeloma, which are often hard to treat and have a poor prognosis.

Dr Stéphane Chevrier and his colleagues in the Molecular Immunology division are interested in understanding the molecular signals that regulate the development of B cells into activated antibody-secreting cells.

Key aspects of this process remain elusive, Dr Chevrier said. "Little is known about the earliest changes that determine the commitment of a B cell to becoming an antibody-secreting plasma cell, and the mechanisms responsible for maintaining these cells in a mature, long-lived state without the cell dying," he said.

The studies will shed new light on regulation of the immune response as well as plasma cell malignancy.

"Identifying new factors involved in this process and improving our knowledge will ultimately aid in the development of more efficient vaccines as well as treatments for autoimmune diseases and cancers, including leukaemia and multiple myeloma," he said.

Dr Chevrier has been with the institute for two years with the support of the Swiss National Science Foundation, first with an 18 month prospective researcher fellowship, and now with an advanced researcher fellowship.

The Swiss National Science Foundation fellowships for advanced researchers enable young scientists planning to follow an academic career to benefit from a stay abroad in order to increase their knowledge and scientific reputation.

Dr Chevrier said he is fortunate to be supported in his studies at the institute.

"Working at the institute is a great opportunity for my scientific career. Without this fellowship that pays for my salary and attendance at conferences, this experience would not be possible," he said.

Dr Stéphane Chevrier

# Publications

**The year ending 30 June 2011 saw the number of scientific papers from the Walter and Eliza Hall Institute reach an 11-year high, with 250 papers published.**

Consistent with previous years, our scientists have published in highly-ranked international journals, including *Nature*, *Science* and *Cell*.

Forty per cent of papers published were in the top 10 per cent of their field, and 9.5 per cent in the top one per cent of their field, according to Thomson Reuters Web of Knowledge, which ranks the impact of journal papers around the world.

A full list of journal papers published this year can be found on the accompanying CD.

Some of our highest impact papers from the year were:

**Super-resolution dissection of coordinated events during malaria parasite invasion of the human erythrocyte.**
Riglar DT, Richard D, Wilson DW, Boyle MJ, Dekiwadia C, Turnbull L, Angrisano F, Marapana DS, Rogers KL, Whitchurch CB, Beeson JG, Cowman AF, Ralph SA, Baum J. *Cell Host Microbe*. 2011 Jan 20; 9(1):9-20.

Malaria is a major infectious disease of the developing world for which there is no current effective vaccine. A critical step in the lifecycle of this parasite is the invasion of red blood cells, where the parasite is protected or 'hidden' from the immune system while it grows and replicates. In this paper, the authors use the latest super resolution microscopy to define the critical events involved in this process, capturing for the first time the malaria parasite invading a red blood cell.

**Mcl-1 is essential for germinal center formation and B cell memory.**
Vikstrom I, Carotta S, Luthje K, Peperzak V, Jost PJ, Glaser S, Busslinger M, Bouillet P, Strasser A, Nutt SL, Tarlinton DM. *Science*. 2010 Nov 19; 330(6007):1095-9.

Memory B cells are essential for the long-lived immunity that arises after immunisation. The germinal centres in the spleen are temporary cell structures where B cells mature and develop immunological memory so that they can respond more quickly when they encounter foreign bodies. For many immune cells a balance between pro-death and pro-survival molecules determines whether they live or die. In this paper it is shown that one particular pro-survival molecule, Mcl-1, is essential for germinal centre function and that this molecule might be a good target for therapies to prevent some types of B cell cancers.

**The transcription factors Blimp-1 and IRF4 jointly control the differentiation and function of effector regulatory T cells.**
Cretney E, Xin A, Shi W, Minnich M, Masson F, Miasari M, Belz GT, Smyth GK, Busslinger M, Nutt SL, Kallies A. *Nature Immunology*. 2011 Apr; 12(4):304-11.

Regulatory T cells are responsible for suppressing the immune response to prevent inflammatory diseases. Disorders that decrease regulatory T cell activity can lead to autoimmune diseases such as type 1 diabetes or coeliac disease, while increased regulatory T cell activity can suppress the immune system when it should be actively killing cancerous or infected cells. In this paper the authors show that two proteins that regulate gene expression (IRF4 and Blimp-1) sequentially induce the maturation of precursor cells into particular types of regulatory T cells, paving the way for potential therapies for autoimmune disease and cancer.

**Comprehensive, quantitative mapping of T cell epitopes in gluten in celiac disease.**
Tye-Din JA, Stewart JA, Dromey JA, Beissbarth T, van Heel DA, Tatham A, Henderson K, Mannering SI, Gianfrani C, Jewell DP, Hill AV, McCluskey J, Rossjohn J, Anderson RP. *Science Translational Medicine*. 2010 Jul 21; 2(41):41-51.

Coeliac disease results from a severe immune reaction in the gut to peptides in wheat, rye and barley. The only current treatment is strict avoidance of these grains in the diet. In this paper, a comprehensive analysis of every possible toxic peptide in gluten revealed that only three peptides account for the inflammatory response in people with coeliac disease, paving the way for development of a vaccine against this disease.

**Germinal center B and follicular helper T cells: siblings, cousins or just good friends?**
Nutt SL, Tarlinton DM. *Nature Immunology*. 2011 Jun; 131(6):472-7.

In this review, the authors describe the intimate relationship between activated B cells and helper T cells, which are involved in activating other immune cells, in the germinal centres of the spleen. This interaction determines the maturation of B cells into antibody-producing plasma cells as well as the formation of long-lasting memory B cells that allow a rapid response to subsequent infectious organisms.

**The golden anniversary of the thymus.**
Miller JFAP. *Nature Reviews Immunology*. 2011 May 27; 11(7):489-95.

Professor Jacques Miller is famed for discovering that the thymus, which had no known function at the time, was essential for development and maturation of T cells. In this history and timeline, Professor Miller recounts the key discoveries that established our current understanding of the division of the immune system into the B cells, which produce antibodies, and T cells which directly kill infected cells and aid in the immune response, as well as how they interact with each other.


**Cells of origin in cancer.**
Visvader JE. *Nature*. 2011 Jan 20; 469(7330):314-22.

In this review, Professor Jane Visvader discusses the evidence that cancers arise from a particular 'cell of origin' – a subset of cell type(s) within an organ – through an initial genetic change, and that multiple further genetic changes result in the mature cancer. It is argued that identifying these 'cells of origin' will help to properly classify tumours and improve our ability to develop new therapeutic strategies to appropriately treat them.

**IL-7 engages multiple mechanisms to overcome chronic viral infection and limit organ pathology.**
Pellegrini M, Calzascia T, Toe JG, Preston SP, Lin AE, Elford AR, Shahinian A, Lang PA, Lang KS, Morre M, Assouline B, Lahl K, Sparwasser T, Tedder TF, Paik JH, DePinho RA, Basta S, Ohashi PS, Mak TW. *Cell*. 2011 Feb 18; 144(4):601-13.

Chronic viral infections such as HIV and hepatitis B and C overwhelm the immune system in early stages of infection, and establish lifelong, persistent infections. Researchers investigated ways to boost the immune response to enable the body to clear virus. In this paper, an immune messenger molecule called interleukin 7 (IL-7) was used to boost the immune response in a mouse model of chronic viral disease. Treatment with IL-7 was able to resolve the infection and limit organ damage by decreasing the levels of SOCS3 (Suppressor of Cytokine Signalling 3), a potent molecule that dampens the immune response.

# Awards

**Staff and students at the institute have been honoured with a number of national and international awards and fellowships this year. These honours included an induction to the Royal Society UK, the Science Minister's Prize for Life Scientist of the Year and an Australia Fellowship.**

Honours and awards received by staff at the institute over the past 12 months include:

Internationally-recognised malaria researcher **Professor Alan Cowman** was elected a Fellow of the Royal Society, the UK's peak academy promoting excellence in science. Professor Cowman has made major contributions to elucidating the mechanisms used by malaria parasites to resist some of the most important antimalarial drugs. This has had implications for the development of new antimalarial treatments and opened the way for surveillance of the geographic spread of drug-resistant strains of malaria.

Cancer researcher **Professor Jane Visvader** received a $4 million Australia Fellowship from the Australian Government to continue her work into the origin of breast, ovarian and lung cancers. Professor Visvader was one of only six scientists awarded the fellowship, which supports medical research with the potential to significantly benefit Australians.

In 2010, institute director **Professor Doug Hilton** was named a Fellow of the Academy of Technological Sciences and Engineering (ATSE). ATSE promotes the development and adoption of existing and new technologies to improve and sustain Australia's society and economy. The academy said Professor Hilton was elected because he "combines excellence in medical research with personal commitment to clinical translation of his discoveries".

Institute biochemist **Dr Colin Ward** was one of 17 new fellows appointed to the Australian Academy of Science. Dr Ward, from the institute's Structural Biology division, has spent many years studying cell surface receptors including the insulin-like growth factor receptor, the insulin receptor, and two members of the epidermal growth factor receptor family.

Structural biologist **Dr Matthew Call** was awarded a $150,000 Victorian Endowment for Science, Knowledge and Innovation (VESKI) Fellowship by the Victorian Government to continue his novel studies of immune cell receptors and signalling. Dr Call focuses on the function and role of the portions of cell signalling receptors that are embedded within cell membranes. His research has the potential to drive development of a new class of drugs for treating autoimmune diseases.

**Dr Chris Tonkin** was named 2011 Victorian Young Tall Poppy of the Year by the Australian Institute of Policy and Science for his work on parasite biology. The Tall Poppy Campaign celebrates Australian scientific and intellectual excellence and encourages younger Australians to follow in the footsteps of outstanding achievers. **Dr Justin Boddey** and **Dr Erinna Lee** were also finalists.

## Solving the mystery of platelets and blood cancers

**Solving a 50-year-old mystery about platelet biology saw Dr Benjamin Kile awarded a Science Minister's Prize for Life Scientist of the Year in 2010.**

Dr Kile, from the Cancer and Haematology division, was presented with the award by the Hon. Kim Carr, Minister for Innovation, Industry, Science and Research. The prize recognises outstanding achievement in science that advances, or has the potential to advance, human welfare.

Dr Kile and his colleagues investigate cancer, stem cells and blood cell production. His major discoveries include research into platelets and platelet lifespan and identification of the normal function of the *Erg* gene, which is linked to many cancers.

Dr Kile said his team showed that *Erg* is a regulator of blood stem cells. "This immediately tells you something about why mutations in *Erg* cause cancer," he said. "Cancers acquire a lot of characteristics of stem cells, so the fact that it is switched on in tumours suddenly made sense."

In 2007, Dr Kile and his institute colleagues received international attention for identifying the molecular program that controls platelet lifespan, transforming the field and solving a 50-year-old mystery about the genes that control whether platelets live or die.

"We discovered that the process is controlled by a pro-survival protein called Bcl-xL and a pro-death protein called Bak. The two are in balance in a healthy platelet, but as it circulates, Bcl-xL slowly runs out, like sand in an hourglass. When the sands runs out, Bak kills the platelet, triggering its removal from the blood."

The discovery raised the prospect of developing new drugs to prolong the shelf-life of platelets stored in blood banks, increasing the availability of this life-saving product for cancer patients and others in danger of serious blood loss or clotting disorders.

Dr Benjamin Kile

# Translation

Associate Professor Clare Scott is searching for new, more effective treatments for ovarian cancer.

# Translating our research

**Translational research continues to move forward at the institute with our strong foundations in basic research being used to transform data and knowledge into meaningful health outcomes through better medical practice.**

Our expanding disease research areas include:

- anti-cancer treatments for breast cancer, ovarian cancer, lung cancer and blood cancers such as leukaemia, lymphoma and multiple myeloma;
- treatments for inflammatory diseases such as rheumatoid arthritis and septic shock, and immune disorders including coeliac disease and type 1 diabetes;
- new vaccines and drugs to target infectious diseases such as malaria, hepatitis B and C, and HIV; and
- personalised medicine, where a patient's treatment is based on their unique clinical, genetic, genomic and environmental circumstances.

The institute encourages, supports and continues to develop clinical collaborations. Fourteen highly skilled clinician-scientists study major diseases and directly link their research findings at the institute to their clinical practice. Through its clinical collaborations, the institute maintains strong links with The Royal Melbourne Hospital, the Royal Women's Hospital and the Peter MacCallum Cancer Centre, as well as other health facilities throughout Australia and internationally.

Our clinician-scientists are also currently involved in more than 80 national and international clinical trials. Many of these trials have achieved significant breakthroughs including a nasal insulin vaccine to treat type 1 diabetes, continued trials and research to support the development of a vaccine for malaria, a new class of anti-cancer drug, and an international phase II trial that has identified a promising new treatment for ovarian cancer.

The institute's highly anticipated new Clinical Translation Centre was completed at the end of June 2011. It is a central facility that will form the cornerstone of translational and clinical research at the institute, providing the essential infrastructure and personnel to expedite the translation of laboratory discoveries into clinical applications.

Clinical Translation Centre staff are, from left: Ms Jenni Harris, Ms Naomi Sprigg, Professor Andrew Roberts and Dr Lina Laskos.

Dr Jason Tye-Din (below right) is a clinical researcher, with a joint appointment at The Royal Melbourne Hospital, who studies coeliac disease.

A Clinical Translation Standing Committee has recently been established with the key goal being identification and removal of barriers to translational research. The committee also provides advice about translational and clinical research to the director and senior management, and assists the head of clinical translation, Professor Andrew Roberts, with the operation of the Clinical Translation Centre. The group also has an essential role in attracting, supporting and retaining medically-qualified researchers at the institute.

This year we held our inaugural translational forum. Focusing on leukaemia and lymphoma, this full-day event brought together more than 60 institute researchers and selected expert external clinicians for presentations and discussions about current laboratory research, clinical updates and strategies for future opportunities and development.

## Coeliac disease vaccine shows promise in phase I trial

**Coeliac disease is a chronic disease caused by an immune reaction to the gluten protein found in wheat, rye and barley. Up to one per cent of the world's population is affected by coeliac disease, which is currently only treatable by eliminating gluten from the diet. In people with coeliac disease, immune cells react to gluten and trigger an immune response that damages the lining of the small intestine and inhibits its ability to absorb nutrients from food.**

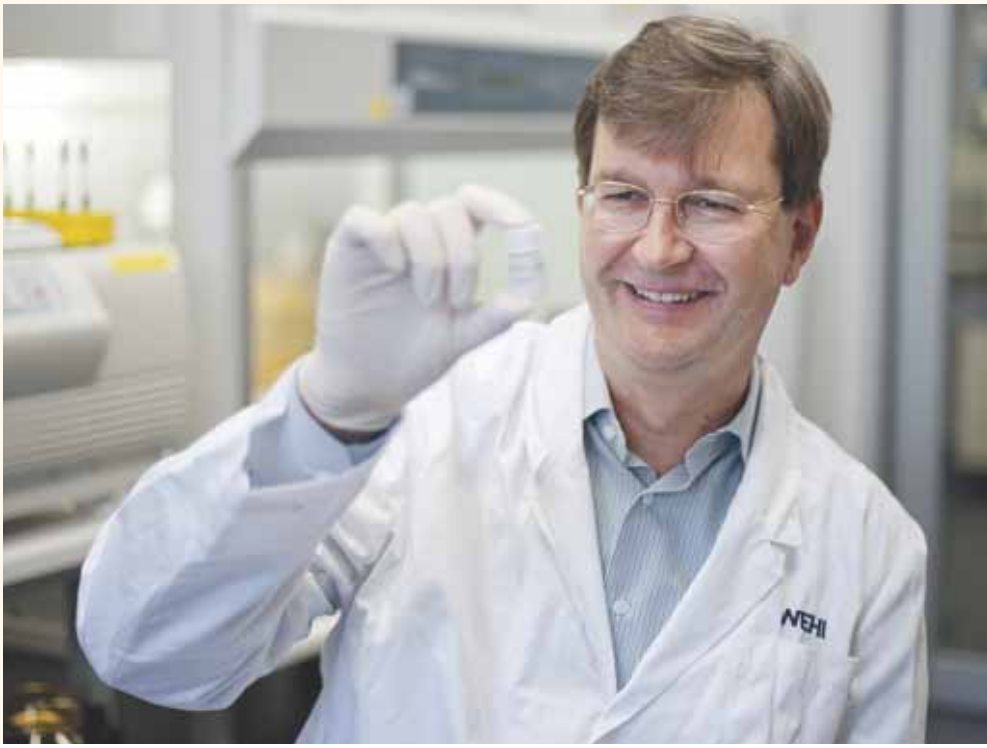
Research by Dr Bob Anderson from the institute's Immunology division has led to the world's first potential vaccine for coeliac disease. A worldwide phase I clinical trial has shown promising results and the vaccine is expected to move to phase II trials within the next year. If successful, the vaccine will be suitable for treating approximately 90 per cent of coeliac disease cases.

The three peptides in gluten on which the vaccine is based were previously discovered by Dr Anderson as being 'toxic' to people with coeliac disease, and form the basis of the coeliac disease vaccine Nexvax2®.

"Our phase I study showed that Nexvax2® was safe to use and well tolerated, and importantly, that it had the desired biological response in patients with coeliac disease," Dr Anderson said. "We expect the vaccine to enter phase II trials by next year, and hope to demonstrate a dramatic reduction in the body's rejection of dietary gluten so patients can resume a normal diet and return to good health."

Nexvax2® is being developed by US biotechnology company ImmusanT, of which Dr Anderson is chief scientific and medical officer. Dr Anderson said the peptides used as part of the vaccine could also be used to improve diagnostic testing of coeliac disease.

"Diagnosing coeliac disease can be quite costly, requiring invasive tests and biopsies to confirm the disease," Dr Anderson said. "The results of a population study suggest that a combination of blood and genetic testing could effectively diagnose coeliac disease without these painful and invasive tests, and reducing costs by up to 50 per cent, which creates a win-win situation."




Dr Bob Anderson heads coeliac disease research at the institute.

# Developing our research

**Building strongly on prior activities, the institute's Business Development Office experienced some major milestones in translating the institute's research in 2010-11. The number of material transfer agreements rose by more than 20 per cent, to 300 for the year, and 85 commercial and collaboration agreements were entered into, a four per cent increase over the previous year.**

Major translation outcomes for the institute this year included:

- advancing the tripartite collaboration with Genentech, a member of the Roche Group, and Abbott to phase I trials;
- teaming up with BD Biosciences for commercialisation of research reagents;
- collaborating with Cancer Research Technology Ltd to progress dendritic cell targeting;
- progression of the target discovery collaboration with CSL;
- completing phase I trials of Nexvax2® for treatment of coeliac disease;
- outcomes from Catalyst Fund investments; and
- completion of the move to in-house patent prosecution.

## Research reagent collaboration

The institute entered into a collaboration with US-based global medical technology company BD Biosciences, a business segment of BD (NYSE:BDX), to evaluate and develop the institute's antibodies for research and diagnostic use. Antibodies are important research and diagnostic tools and this collaboration will ensure a strong focus on making the institute's research tools commercially available. Several antibodies have already been selected for commercialisation. The partnership builds on our programs focused on identifying novel targets for therapeutic monoclonal antibody and drug development, many involving development of new antibodies through the institute's in-house monoclonal antibody facility.

## Dendritic cell targeting and Clec9A

Our agreement with Cancer Research Technology Ltd, the technology transfer company of Cancer Research UK, for the cross licensing and commercialisation of Clec9A-related dendritic cell-targeting intellectual property has significantly enhanced our ability to develop a novel vaccine platform for cancers and infectious diseases. Clec9A is a molecule on the surface of CD8+ dendritic cells that could dramatically enhance the immune response in both cancer and infectious diseases. Combining the previously competitive approaches to translation of Clec9A meant that we were able to move quickly to 'proof-of-concept' using an HIV model, thus enhancing the possibility of finding a development partner.

## CSL collaborations

Our strategic translation relationship with CSL progressed strongly during the year with late pre clinical progression of the G-CSF (granulocyte colony stimulating factor) antagonism program for treating inflammatory diseases based on discoveries in the institute's Reid Laboratory, headed by Professor Ian Wicks. The collaborative target discovery program based on a systems biology approach to identifying novel drug targets resulted in the discovery of several new potential drug targets. This program was expanded during the year through successful securing of funds from the CSIRO Science Industry and Endowment Fund (SIEF) to carry out a parallel target discovery program in blood stem cells. The program aims to develop agents for stem cell mobilisation and develop methods for *in vitro* platelet production.

## Coeliac disease vaccine completes phase I trials

The start-up company Nexpep Pty Ltd successfully completed a phase I clinical trial of Nexvax2®, a peptide-based vaccine designed to induce tolerance to gluten, the protein that causes coeliac disease. Nexpep transferred its assets to US-based ImmusanT which was specifically created to commercialise the technology through access to US capital markets. Basic research headed by Dr Bob Anderson will continue at the institute and a new collaborative agreement has been executed with ImmusanT.

Dr Julian Clark

### Catalyst Fund delivers

In its second year of operation, the Business Development Office Catalyst Fund for 'proof–of-concept' trials of new translation opportunities achieved returns well in excess of the investment and has enabled progression of several promising projects.

Investments included a new class of kinase inhibitors for treating solid tumours, dendritic cell-targeting technology for infectious disease and cancer therapy, potential antagonists of IGF-1R as tool compounds and cancer drugs, a new platform for the production of antibodies that are extremely difficult to produce, particularly for autoimmune conditions, and demonstrating that a soluble cell surface molecule has immune regulating properties and is a potential biological agent for therapy of inflammatory diseases.

### Patent prosecution

The first full year's results from in-house patent prosecution confirm the benefits of increased service level, improved accuracy and reduced expenses. The direct use of foreign attorneys has provided better access to information on changes to examination procedures, more time to consider office actions and less requests for an extension of time to respond. With a strategy driven by the expertise and experience represented by the Business Development Office's intellectual property group, we develop direct relationships with our attorney counterparts in key territories.

## Institute discovery leads to clinical trials of new cancer drug

**Chronic lymphocytic leukaemia (CLL) is the most common type of leukaemia in Australia. It is a disease of the white blood cells that develops over months or years, and is most common in adults. One in 176 Australians will be diagnosed with CLL by the age of 85.**

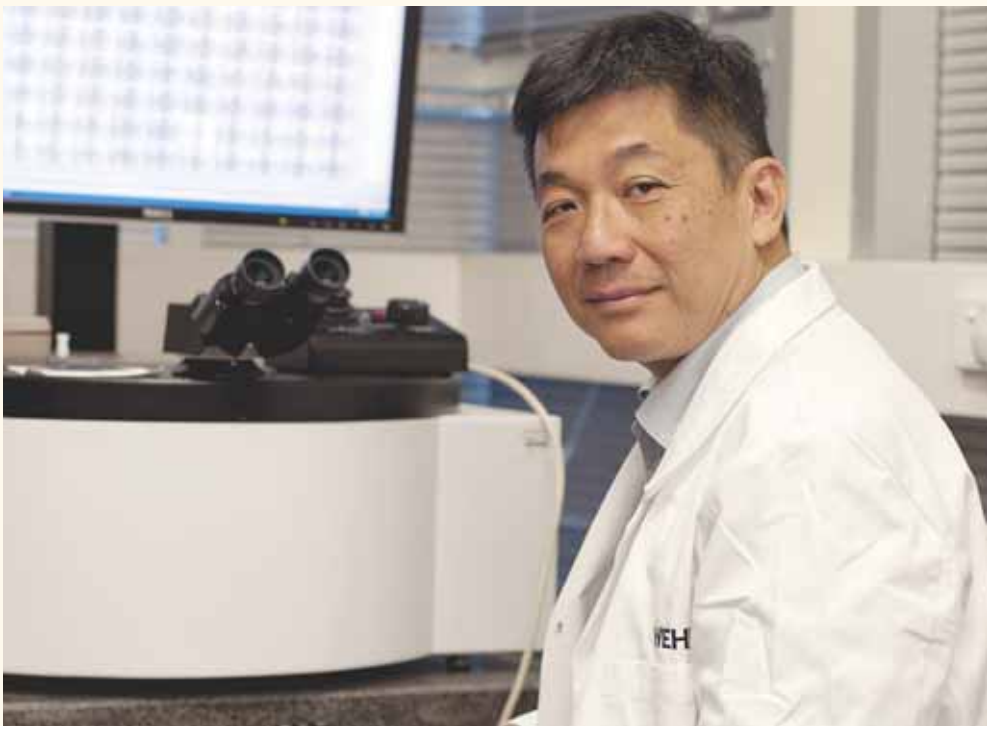
A scientific discovery made 20 years ago at the Walter and Eliza Hall Institute has led to the development of a potential new anti-cancer agent, ABT-199 (GDC-0199/RG7601), that is now entering clinical trials to treat CLL. ABT-199 is a so-called 'BH3-mimetic' drug, which is designed to block the function of the protein Bcl-2, making leukaemia cells vulnerable to programmed cell death.

The cancer-causing role of Bcl-2 was first discovered at the institute by then-PhD student and current deputy director Professor David Vaux, with Professors Suzanne Cory and Jerry Adams. Bcl-2 is a pro-survival protein, preventing cells from undergoing programmed cell death (apoptosis) after injury. Bcl-2 is over-expressed in a number of cancers, including CLL, and research at the institute over the past two decades has explained much about how Bcl-2 and related molecules function to determine if a cell lives or dies.

ABT-199 was co-developed for clinical use by two companies, Abbott and Genentech, and was discovered in a joint research collaboration that also involved scientists at the Walter and Eliza Hall Institute. Patients with CLL have begun to receive the agent ABT-199 as part of a worldwide phase Ia clinical trial coordinated locally by Cancer Trials Australia.

Institute director Professor Doug Hilton said this collaborative arrangement enhanced the institute's ability to rapidly translate its laboratory discoveries into benefits for patients. "The institute has supported research teams that are dedicated to improving outcomes for patients," he said. "In this case we are seeing more than two decades of research culminating in what we hope will be a promising new drug."

The head of business development at the institute, Dr Julian Clark, described the collaboration with Abbott and Genentech as unique. "The combination of large biotech and pharmaceutical companies with an academic research institute is regarded as the industry benchmark," he said. "We anticipate that other compounds discovered at the institute will be able to enter clinical trials through similar collaborative efforts."



Professor David Huang, who heads the Chemical Biology division, in the institute's high-throughput chemical screening facility.

# Patents granted in 2010–2011

### A method of treatment and prophylaxis

**Inventors:** K Lawlor, I Wicks, I Campbell, A Roberts, D Metcalf
*Australia and Japan*

### A method of diagnosis and treatment and agents useful for same

**Inventors:** J Visvader, G Lindeman, E Sum, L O'Reilly
*Japan and New Zealand*

### Modified cells that co-express Blimp1 and a reporter molecule and methods of using the same

**Inventors:** A Kallies, J Hasbold, D Tarlinton, L Corcoran, P Hodgkin, S Nutt
*Australia*

### Alpha-helical mimetics

**Inventors:** G Lessene, J Baell
*United States*

### Therapeutic agents and uses thereof

**Inventors:** M O'Keefe, K Shortman, B Francke, L Harrison, R Steptoe, D Vremec
*Europe and New Zealand*

### A method of cell isolation

**Inventors:** G Lindeman, J Visvader, M Shackleton, F Vaillant
*Australia*

## Protecting our assets

**The second major annual laboratory notebook audit was conducted by the Business Development Office during the year.**

Compliance with international laboratory notebook standards is essential if the institute is to capture and exploit its intellectual property, and be compliant with the expectations of our translation partners who expect our standards of documentation to be commensurate with our reputation for research.

The audit spanned 47 laboratories, included 228 scientists and revealed a significant improvement in compliance, with 41 per cent of scientists' notebooks being rated as 'excellent'. During the year 56 per cent of the institute's laboratories were engaged in collaborative research with industry. Importantly, all laboratories having commercial collaborations had compliant notebooks. Laboratory and division heads were given feedback and we look forward to this being an annual event.

Dr Tricia Diggle (far left) and Ms Carmela Monger from the Business Development Office discuss laboratory notebook compliance with Dr Grant Dewson (centre).

# Education

Dr Guillaume Lessene (above left) and Honours student Mr Michael Roy, from the Chemical Biology division.

# Education

**The Education Committee is reflecting on a productive and rewarding year, which derives from the pleasure of working with bright young people and seeing them grow as individuals and as scientists.**

The institute currently has 80 PhD students and 15 Honours students and has hosted 20 Undergraduate Research Opportunities Program (UROP) students, 18 overseas research trainees and nine vacation students over the past 12 months. Ten PhD students completed their degree in the past year. Our congratulations go to Drs Ryan Brady, Duncan Carradice, Carolyn de Graaf, Shirley Elkassaby, Sarah Kinkel, Hiu Kiu, Catherine Nie, Sarah Oracki, Jonathan Richards and Hua Yu on this achievement.

We were fortunate to have an exceptional group of Honours students in 2010. All 21 students of the 2010 Honours cohort achieved first-class honours. Congratulations go to our top 2010 Honours student, Ms Hannah Vanyai, for being named on the Dean's Honour List for the Faculty of Science.

Congratulations also to Alan Yap, who was the successful recipient of the Cyril and Paddy Pearl Scholarship. This PhD scholarship was established in 2010 by the late Mrs Paddy Pearl in memory of her late husband, Cyril. Alan is undertaking his PhD in the Infection and Immunity division, investigating the role of proteins that remodel red blood cells after malaria invasion.

This year's Harold Mitchell Foundation travel awards went to PhD student Sarah Oracki and postdoctoral scientist Luke Pase. Ms Oracki used her fellowship to attend the 5th International Conference on Gene Regulation in Lymphocyte Development as well as visit laboratories in London, Boston and New York. Dr Pase used his fellowship to attend the European Molecular Biology Organization (EMBO) Conference on Molecular and Cellular Basis of Regeneration and Tissue Repair as well as visit several leading European institutes to explore postdoctoral opportunities.

A major task in the past year has been planning new Honours coursework. As a consequence, our 2011 Honours students enjoyed the benefit of a new Experimental Design and Statistics course taught by Professor Terry Speed and colleagues from the Bioinformatics division, as well as Professor David Vaux and Dr Anne Voss. The students also undertook a quarter of advanced coursework in The University of Melbourne's Department of Biochemistry. In return, Department of Biochemistry Honours students participated in the institute's Experimental Design and Statistics course. The mutual teaching arrangements have broadened and enriched the experiences of students in both departments, with early feedback suggesting the new coursework was a success and a challenge to the students.

One of our explicit aims is to encourage medical professionals to participate in laboratory-based research, as clinician-scientists form an important link for knowledge translation between basic science and clinical care. Our recent initiatives in this area include the establishment of a small scholarship for medical students who interrupt their studies briefly to engage in laboratory-based research at the institute. A second development is an internal PhD scholarship to accommodate exceptional candidates who are medical graduates and passionate about laboratory research.

PhD students Maya Olshina (left) and Alex Delbridge

## Malaria parasite caught red-handed invading blood cells

**Each year the malaria-causing *Plasmodium* parasite infects more than 400 million people worldwide, and as many as a million people, mostly children, die from malaria.**

Mr David Riglar, a PhD student working with Dr Jake Baum in the Infection and Immunity division, has for the first time captured images of malaria parasites in the act of invading red blood cells.

The malaria parasite is only one micron (one millionth of a metre) in diameter, and in the past it has been difficult both to infect red blood cells with the parasite in the laboratory, and to capture images of this process.

Mr Riglar and colleagues developed new ways to study parasites during the invasion process. They collaborated with researchers from the ithree institute at the University of Technology, Sydney, to reliably capture high-resolution images of the parasite at each and every stage of invasion. This was achieved using a combination of electron, light and super resolution microscopy – a technology platform new to Australia.

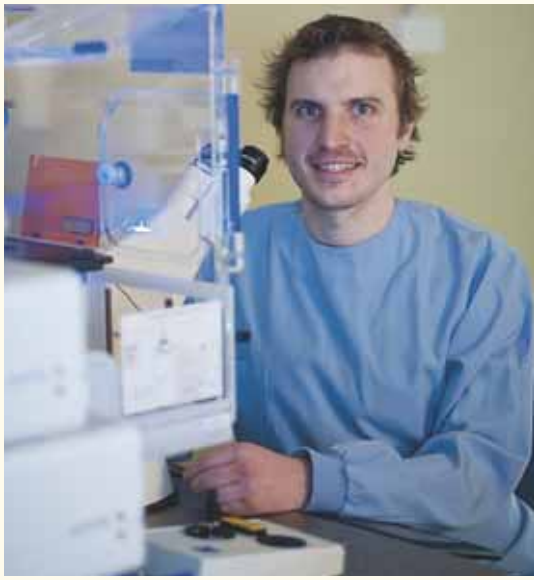
"These innovative imaging techniques have allowed us to observe the invasion process at a molecular level that has never been seen before," said Mr Riglar. "There are many proteins that we know are involved in the invasion process, but we don't know precisely where they are positioned, or how they act. Now we can start to answer some of these questions, which will be really exciting for malaria researchers worldwide.

"Being able to clearly see each separate stage of invasion with this level of detail will also help us to precisely determine how antimalarial drugs or vaccines stop the parasite from entering the red blood cell. In the future, new treatments for malaria may be designed to stop particular stages of the invasion process," he said.

**Collaborating institution:** ithree institute, the University of Technology, Sydney.

**Funding partners:** National Health and Medical Research Council, The University of Melbourne (Pratt Foundation Scholarship), Canadian Institutes of Health, University of Technology, Sydney, Australian Research Council and the Victorian Government.

**More information:** Riglar DT, Richard D, Wilson DW, Boyle MJ, Dekiwadia C, Turnbull L, Angrisano F, Marapana DS, Rogers KL, Whitchurch CB, Beeson JG, Cowman AF, Ralph SA, Baum J. Super-resolution dissection of coordinated events during malaria parasite invasion of the human erythrocyte. *Cell Host Microbe*. 2011 Jan 20; 9(1):9-20.



PhD student Mr David Riglar

## Uncovering the molecular control of airway development

**The development of a mammal requires every organ and structure to be formed in the correct location within the embryo. This process is precisely controlled by the actions of thousands of genes.**

Genetic defects that hinder proper embryonic development are seen in human conditions such as DiGeorge Syndrome, in which blood vessels and organs in the head, neck and upper chest cavity are not correctly formed.

The control of embryonic development by the *Moz* gene was the focus of Ms Hannah Vanyai's Honours research in the Molecular Medicine division, supervised by Drs Anne Voss and Tim Thomas.

Ms Vanyai's project examined whether MOZ controls the development of structures in the head, neck and chest. "We found that the size of the upper airways, especially the nasal passage, requires the correct expression of *Moz* in a particular region of the early embryo called the neural crest," she said.

"This is the first time that a single gene has been linked to the control of airway size. We can now begin to understand the molecular machinery that drives airway development."

Ms Vanyai was the top Honours student in The University of Melbourne Department of Medical Biology in 2010, and was named on the Dean's Honour List for the Faculty of Science. As a PhD student at the institute, Ms Vanyai is continuing to define how *Moz* regulates airway development.

Honours student Ms Hannah Vanyai

# 2010–2011 graduates

**The following students successfully completed their studies in the past year:**

## Doctor of Philosophy, The University of Melbourne

### Dr Ryan Brady
Benzoylureas as BH3-only peptide mimetics: design, synthesis and conformational constraints.
*Supervisors: Dr J Baell, Dr G Lessene and Professor R Norton*

### Dr Duncan Carradice
Genetic basis of congenital myeloid failure syndromes in mutant zebrafish.
*Supervisors: Dr G Lieschke and Dr J Layton*

### Dr Carolyn de Graaf
Genomic analyses of haemopoiesis.
*Supervisors: Professor D Hilton, Dr G Smyth and Dr L Wu*

### Dr Shirley Elkassaby
Effects of vitamin D on immune and metabolic function in humans.
*Supervisors: Professor L Harrison, Dr S Fourlanos and Dr J Dromey*

### Dr Sarah Kinkel
Regulation of promiscuous expression in medullary thymic epithelial cells.
*Supervisors: Dr M Blewitt, Dr W Heath, Dr H Scott and Professor D Hilton*

### Dr Hiu Kiu
The role of SOCS3 and related proteins in inflammatory processes.
*Supervisors: Professor A Roberts and Professor W Alexander*

### Dr Catherine Nie
Leukocyte trafficking in the control of disease and immunity to malaria.
*Supervisors: Dr D Hansen and Dr L Schofield*

### Dr Sarah Oracki
Resolving causes and consequences in a model of autoimmune disease.
*Supervisors: Dr D Tarlinton and Dr S Nutt*

### Dr Jonathan Richards
The role of antibodies to merozoite antigens in protection from symptomatic *Plasmodium falciparum* infection.
*Supervisors: Dr J Beeson and Professor G Brown*

### Dr Hua Yu
Investigation of autoreactive T cells in type 1 diabetes.
*Supervisors: Professor L Harrison, Dr S Mannering and Dr A Lew*

## Bachelor of Science (Honours), The University of Melbourne

### Natasha Anstee
The impact of Bcl-2 versus Mcl-1 overexpression in haemopoietic cells.
*Supervisors: Dr K Campbell, Dr C Vandenberg and Professor S Cory*

### Fiona Bell
Monitoring Bak and Bax activation and oligomerisation in live cells.
*Supervisors: Dr R Kluck and Dr G Dewson*

### Bianca Capaldo
Definition of transcriptional regulators of commitment and differentiation of mammary progenitor cells.
*Supervisors: Professor J Visvader and Professor G Lindeman*

### Shih Chieh Chang
Novel potassium channel blockers for the treatment of autoimmune diseases.
*Supervisors: Professor R Norton and Dr C Galea*

### Kelan Chen
Structure-function analysis of the epigenetic regulator protein, SmcHD1.
*Supervisors: Dr J Murphy and Dr M Blewitt*

### Monica Diviak
How does apoptosis regulate autoimmune mediated tissue inflammation?
*Supervisors: Professor I Wicks and Dr K Lawlor*

### Freya Kahn
Targeting apoptosis for treating cancer.
*Supervisors: Professor D Huang and Professor A Roberts*

### Anastasia Kurniawan
Inflammatory mediators of insulin resistance in human obesity.
*Supervisors: Dr J Wentworth and Professor L Harrison*

### Stephen Ma
Elucidating the Bak apoptotic pore complex.
*Supervisors: Dr R Kluck and Dr G Dewson*

### Julia Marchingo
The effect of co-stimulation on T-cell dynamics.
*Supervisors: Professor P Hodgkin and Dr S Heinzel*

### James McCoy
Functional characterisation of calcium-dependent protein kinases in *Toxoplasma* host cell invasion.
*Supervisors: Dr C Tonkin and Dr J Baum*

### Lewis Murray
Role of natural killer receptors in the control of malaria pathogenesis.
*Supervisors: Dr D Hansen and Dr L Schofield*

### Blazhe Nedanovski
Reversing the drug resistance observed in mouse lymphomas which overexpress Polycomb genes.
*Supervisors: Dr C Scott and Dr M Wakefield*

### Victoria Ryg-Cornejo
Role of T cell homing in the control of pathogenesis and immunity to malaria.
*Supervisors: Dr D Hansen and Dr L Schofield*

### Lisa Sampurno
Programmed cell death and angiogenesis.
*Supervisors: Dr L Coultas and Professor A Strasser*

### Joanne Slater
Function of BCL2 family proteins in zebrafish.
*Supervisors: Dr G Lieschke and Dr L Pase*

### Hannah Vanyai
The role of the monocytic leukaemia zinc finger protein (Moz) in embryonic development.
*Supervisors: Dr A Voss and Dr T Thomas*

### Hong Juan Wu
Calcium regulation in *Toxoplasma gondii* host cell invasion.
*Supervisors: Dr C Tonkin and Professor A Cowman*

### Alan Yap
Role of T cells and the spleen in the aetiology of severe malarial anaemia.
*Supervisors: Dr L Schofield and Dr D Hansen*

### Janet Yeo
Transcriptional regulation of immune cells of the gut.
*Supervisors: Dr G Belz and Dr S Nutt*

### Elizabeth Zuccala
Cell-cell interactions during malaria parasite invasion of the human erythrocyte.
*Supervisors: Dr J Baum and Professor A Cowman*

# Seminars

**The Wednesday seminar series provides a forum for the best research at the institute to be showcased before the entire scientific staff while also providing a platform for visiting researchers to present their work.**

This year we hosted 40 seminars in the Wednesday series, which included five guest speakers in addition to representatives from all of the institute's divisions, at all career levels. We also had eight PhD students present at the Wednesday forum.

A slight change to the format this year was the inclusion of a number of laboratory heads giving overviews of their recent achievements and plans for the near future. One of the institute's newest laboratory heads, Dr Marie-Liesse Asselin-Labat from the Stem Cells and Cancer division, presented her work on the breast cancer stem cell, an area of great current interest.

From our more senior ranks Professor Jerry Adams, who is joint head of the Molecular Genetics of Cancer division, gave an overview of the molecular causes of cancer, highlighting how the work into apoptosis from his division over many years has facilitated the development and testing of potent novel anti-cancer therapies.

Among our guests, we were fortunate to host Professor Meinrad Busslinger from the Research Institute of Molecular Pathology, Vienna, Austria. Professor Busslinger is a member of the institute's Scientific Advisory Board and presented an outstanding talk describing his long, successful and technically sophisticated analysis of lymphocyte development.

We also had former institute students return to present talks about their current research. This included Dr Shalin Naik, now at the Netherlands Cancer Institute, who presented a most exciting insight from his work on a sophisticated approach, called bar-coding, that tracks cell differentiation in complex systems. Dr Naik is using this approach to track the development of white blood cells.

A full list of institute seminars held in 2010-11 are on the accompanying CD.


Institute board member Dr Graham Mitchell addressing attendees at the function held to celebrate the 50th anniversary of the discovery of the function of the thymus.

# Institute awards

## The Burnet Prize

**Dr Marie-Liesse Asselin-Labat from the Stem Cells and Cancer division was awarded the Burnet Prize in 2010, the institute's top award.**

The prize has been awarded annually since 1987 and was established through a bequest from Sir Macfarlane Burnet (institute director 1944-65). It acknowledges exceptional achievement by early-career researchers.

Dr Asselin-Labat received the award for her studies of breast stem cells and their role in some types of breast cancer. She discovered that breast stem cells are exquisitely sensitive to the female hormones oestrogen and progesterone. The finding explains decades of evidence linking breast cancer risk to exposure to female hormones, and opens the way for the development of new preventions and treatments for breast cancer.

In 2011, Dr Asselin-Labat was selected to establish her own laboratory within the Stem Cells and Cancer division. Her laboratory will focus on lung cancer and the cells that lead to the development of lung cancer.

"I'm interested in looking at how lung stem cells are regulated and what drives tumour initiation in the lungs," she said. "There is a real need for research into lung cancer."

## The de Burgh Fellowship

**This year the institute established the de Burgh Fellowship to honour the role Professor Patrick de Burgh played in shaping the institute. Professor de Burgh was an infectious disease researcher. He died at the age of 94 on 1 August 2010.**

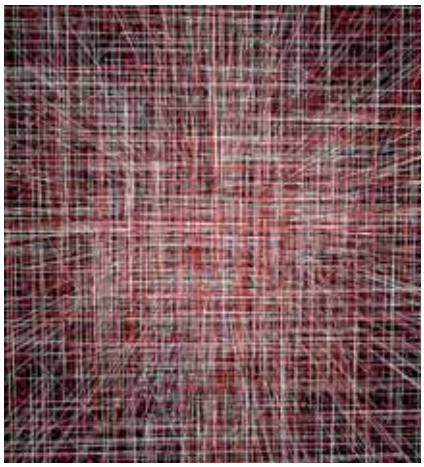
It was in Professor de Burgh's laboratory at the University of Sydney that institute legends Professor Donald Metcalf, Professor Jacques Miller and Sir Gustav Nossal obtained their first taste of research.

**Dr Guillaume Lessene** from the institute's Chemical Biology division was the inaugural recipient of the de Burgh Fellowship.

Dr Lessene translates research findings from the institute into the discovery and development of new drugs. His main focus is cancer research and Dr Lessene is currently working on developing inhibitors to the pro-survival Bcl-2 proteins that are involved in programmed cell death, for treatment of several types of cancer. He is also involved in projects looking at other cancer targets, such as tyrosine kinases, and non-cancer targets involved in conditions such as Alzheimer's disease.

Dr Marie-Liesse Asselin-Labat

Dr Guillaume Lessene



Dr Brian Smith's 'Molecular Plaid'

### The institute's other award winners were:

**Best seminar:** The 2010 Seminar Prize was a three-way tie between **Dr Justin Boddey** from the Infection and Immunity division for his presentation 'Export of malarial virulence proteins that remodel parasitised human erythrocytes', **Dr Stefan Glaser** from the Cancer and Haematology division for his presentation 'Role of pro-survival Bcl-2 family members in acute myeloid leukaemia', and **Dr John Wentworth** from the Autoimmunity and Transplantation division for his presentation 'Inflammation in diabetes: cause or consequence?'.

**Art in Science Prize: Dr Brian Smith** from the Structural Biology division was awarded the Art in Science Prize for his image 'Molecular Plaid', a striking image that shows the dynamics of molecules of water.

Three awards were given for 25 years service to the institute: **Ms Heather Orange** and **Ms Josie Pink** from Preparation Services, and **Mr David Vremec** from the Immunology division.

# Engagement

Students from Ivanhoe Girls' Grammar School on a discovery tour at the institute's Bundoora campus.

# Engagement

**One of the key goals of the institute is to drive community conversations about science and the benefits of medical research for public health and wellbeing.**

We strongly believe that fostering an open dialogue about Australian research and innovation will help advance debates into the 21st century on the future of science and medical research.

Institute staff and students have embraced the opportunity to share their interest in science. This has ranged from participating in the activities of science and biotechnology organisations, to joining grant review panels, and serving on the boards and committees of organisations across the medical research sector. Our public engagement has stretched beyond this, with institute staff and students sharing their knowledge and time with schools, community groups, donors, bequestors and the wider community to keep them informed of the latest institute research and achievements.

This year, we had a large increase in discovery tours on offer to the public, with 700 people across 30 groups attending.

Two public lectures were also held: in December 2010 Professor Andrew Roberts shared his knowledge on blood cancers and the latest developments in treatment, while in March 2011 Dr Marc Pellegrini spoke on the topical issue of infectious disease and antibiotic-resistant bacteria. More than 300 people attended these lectures.

The institute was also represented at The University of Melbourne Festival of Ideas, a biennial public lecture program intended to stimulate and inform community discussions. The theme for the 2011 Festival of Ideas was 'The Pursuit of Identity: Landscape, History and Genetics'. Institute director Professor Doug Hilton spoke as part of the session 'The Genetic Revolution: Health and Human Identity', chaired by former institute director Professor Suzanne Cory.

In the past 12 months the institute has joined the social media revolution, establishing a presence on Facebook, LinkedIn and Twitter. Institute director Professor Doug Hilton also joined the conversation on Twitter – follow @WEHI_Director for his updates. These social media sites have given us a unique opportunity to connect with people nationally and internationally, and keep up-to-date on the latest news in the sector as well as engage with our supporters.

A major highlight of the first half of 2011 was the institute-led Discoveries Need Dollars campaign. The campaign was instigated by the institute following reports that the federal government planned to significantly cut medical research funding in the federal budget. We were overwhelmed by the community support for the campaign, which attracted an enormous amount of interest and action from not only scientists but also community members who were concerned about the potential outcomes of funding cuts for finding cures and treatments for disease. The campaign was successful, with the budget being maintained and a review of the medical research sector being announced.

Researchers and the community rally for research in Melbourne as part of the institute-led Discoveries Need Dollars campaign.

# Strategic partners

**Collaborative research partnerships are at the heart of much of the research carried out at the institute. We place a high priority on research collaborations that support the institute's mission of 'Mastery of Disease Through Discovery'.**

Many of our collaborations help to ensure that fundamental discoveries made in the laboratory are translated to the clinic. The Walter and Eliza Hall Institute has been involved in a number of initiatives to drive collaboration in medical research in Australia.

The **Victorian Breast Cancer Research Consortium**, established in 1997, is a consortium of eight Melbourne medical research institutes and the Cancer Council Victoria. It is a major funding source for the activities of the institute's Stem Cells and Cancer division, and was responsible for the long-term funding that aided in the discovery of breast stem cells, which are believed to play a role in the development of breast cancer.

The **Victorian Cancer Biobank** has also been a major contributor to the Stem Cells and Cancer division's research, providing human breast tumour tissue that enables our researchers to make new discoveries about the biology of breast cancers. In 2011, the collaboration led to the discovery by Professors Geoff Lindeman and Jane Visvader that a new class of anti-cancer agents called BH3-mimetics show promise for treating breast cancers that over-express the pro-survival Bcl-2 protein, including cancers with poor prognosis.

As a supporting member of the **Hearing Cooperative Research Centre,** the institute is working to better understand age-related and acquired forms of hearing loss. This work aims to develop better diagnostic tools and to identify molecules that may be targeted by drugs for the prevention and treatment of hearing loss. A genome-wide screen for mutations causing progressive hearing loss in mice has yielded 18 new genetic models of this condition. The hearing group is also investigating the regulation of cell death in the auditory system as a potential avenue for intervening in the disease. Understanding the complex molecular events that contribute to onset and progression of cochlear degeneration will help us to design targeted therapeutic and preventive strategies for hearing impairment.

## Medical Research Commercialisation Fund

**The Medical Research Commercialisation Fund (MRCF), founded in 2007, provides funding to its member institutes for the early-stage development of medical technologies with commercialisation potential. These include the discovery of drug compounds and proof-of-principle projects.**

The Walter and Eliza Hall Institute has been a member of the MRCF since 2007.

The MRCF was established through collaboration between medical research institutes and allied research hospitals across Australia. The collaborative fund is supported by the state governments of Victoria, New South Wales, Queensland and Western Australia. It currently has 27 members.

In 2010 BACE Therapeutics, a company formed by the Walter and Eliza Hall Institute, The University of Melbourne, Mental Health Research Institute and SYNthesis Med Chem, successfully secured $650,000 in funding from the MRCF with the support of the Victorian Government to implement the preclinical development of candidate compounds for the treatment of Alzheimer's disease.

Alzheimer's disease is the most common form of dementia in the elderly, affecting more than 18 million people globally. Although some therapies exist to ease the symptoms, there is no current treatment to treat the disease or stop disease progression.

Dr Brian Smith from the institute's Structural Biology division identified two compounds that bind the enzyme beta secretase (also called BACE-1), which is elevated in parts of the brain of Alzheimer's patients. The observation of elevated beta secretase in Alzheimer's was initially made by Dr Genevieve Evin from The University of Melbourne and, working collaboratively, Drs Smith and Evin have shown the two compounds are effective in blocking the activity of beta secretase potentially slowing or even blocking the progression of Alzheimer's.

As part of its capacity-building goal, MRCF runs a trainee/secondment program for staff of member institutes to develop first-hand experience with investment management and venture capital processes. Dr James Dromey from the Business Development Office was the first institute staff member to take part in this program, completing it in August 2010.

Dr James Dromey from the institute's Business Development Office participated in the MRCF trainee/secondment program.

# Scientific and medical community

**In addition to their research workloads, our scientists contribute to the scientific and medical community in a variety of ways, both nationally and internationally.**

This includes serving on review panels, boards and committees, undertaking editorial work for scientific and medical journals, conference organisation and attendance, and involvement with biotechnology and clinical advisory groups and public health programs.

This year, our scientists undertook engagement with the medical and scientific communities in the following ways:

Institute scientists served on the boards and committees of organisations including the European Molecular Biology Organization, Pasteur Institute (France), Wellcome Trust Sanger Institute (UK), Wellcome Trust Centre for Human Genetics (UK), Cambridge Research Institute (UK), and National Institutes of Health TrialNet (US).

Faculty members assisted in evaluating research grants and participated in grant review panels for the National Health and Medical Research Council, Australian Research Council, Cancer Council Australia, National Institutes of Health (US), Cancer Research UK, Juvenile Diabetes Research Foundation (Australia), Wellcome Trust (UK), Pfizer Australia, European Research Council, Canadian Foundation for Innovation, Swiss National Research Council and Medical Research Council (UK).

Our researchers have also sat on editorial boards for international science journals such as *Proceedings of the National Academy of Sciences of the USA, Journal of Immunology, Cancer Research, International Journal of Haematology, Cell Stem Cell, Cell Death & Differentiation* and *Oncogene*.

Our staff have engaged with the biotechnology industry as advisers, consultants and committee members for organisations including the Bio21 Cluster, Cancer Council Victoria, CSL Ltd, GlaxoSmithKline Biologicals, ImmusanT Inc, Malaria Vaccine Initiative of PATH/MVI, National Breast Cancer Foundation, Victorian Breast Cancer Research Consortium and the Victorian Cancer Agency.

More details on our engagement with the scientific community is on the accompanying CD.

## Institute hosts government grants announcement

**The institute hosted some of Australia's leading scientists in March when the National Health and Medical Research Council (NHMRC) chose the institute as the site for its annual announcement of program grant funding.**

The Hon. Mark Butler MP visiting the institute to announce $107 million in NHMRC funding.

Federal Minister for Mental Health and Ageing the Hon. Mark Butler MP, and NHMRC chief executive officer Professor Warwick Anderson attended the event, to announce $107 million in funding for nine high-calibre, collaborative projects designed to improve health and wellbeing in Australia.

The institute received $38.4 million in funding as part of the announcement. The funding will support collaborative studies that will extend current institute research into blood cells and cancer. Division heads Professor Nick Nicola from the Cancer and Haematology division and Professor Jerry Adams from the Molecular Genetics of Cancer division are leading the two funded programs.

Several other representatives from the Department of Health and Ageing and NHMRC committee attended the event, as well as grant recipients from The University of Melbourne, Australian National University, Children's Cancer Institute Australia, National Stroke Research Institute, Queensland Institute of Medical Research and The University of Sydney.

The NHMRC program grants scheme provides support for teams of high-calibre, internationally-competitive researchers who pursue broad, collaborative research.

Institute director Professor Doug Hilton said the NHMRC's program grants scheme provided vital support for Australian researchers to tackle complex but important research questions that might take many years to unravel.

"The program grants scheme is recognition that if Australian scientists are to continue to make discoveries that benefit human health they require sustained and significant support that brings together large research teams from diverse areas of medical research," Professor Hilton said.

## Continuing links with the World Health Organization

**The World Health Organization (WHO) has renewed the institute's status as a WHO Collaborating Centre for Research and Training in Immunology and Molecular Parasitology until 2014.**

Professor Alan Cowman, who heads the centre, said it is an important extension of the institute's malaria research program. "Our collaboration with WHO will enhance the development of new vaccines to prevent malaria, a disease that kills more than one million people every year, most of whom live in developing countries. One important aspect is that it assists our scientists in accessing valuable malaria patient samples from malaria-endemic countries," Professor Cowman said.

The collaboration also enables the institute to train researchers and field workers from malaria-endemic countries. In 2010 Mr Jack Taraika from the Papua New Guinea Institute of Medical Research (PNGIMR) spent two months at the institute to learn flow cytometric techniques, and in 2011 Ms Elisheba Malau, also from PNGIMR, undertook Honours research at the institute, supervised by Drs Ivo Mueller and Alyssa Barry in the Infection and Immunity division.

The WHO collaboration also supported the attendance of several PNGIMR researchers at the International Congress of Parasitology in 2010, and enabled institute researchers to conduct a biostatistics course at the PNGIMR in 2011.

Professor Mueller, who taught at the biostatistics course, said the institute's WHO Collaborating Centre status was especially important for training researchers and building capacity in our malaria-endemic partner countries - Papua New Guinea, the Solomon Islands and South-East Asia. "Building links with scientists in malaria-endemic areas is a critical aspect of ensuring that research conducted at the institute is maximally relevant to improving the treatment and prevention of this disease," he said.

Course instructors Professor Ivo Mueller (Infection and Immunity division, front left) and Katie Benton (Stanford University, back left) with participants in the biostatistics course held at the Papua New Guinea Institute of Medical Research. *(Photo credit: Katie Benton)*

## Quintuple anniversary celebrates science legends

**On Thursday 2 June 2011, the Walter and Eliza Hall Institute hosted more than 200 alumni and invited guests from around the world to celebrate a quintuple anniversary of science legends.**

The quintuple anniversary celebration recognised the 50th anniversary of the discovery of the function of the thymus by institute researcher Professor Jacques Miller. It also honoured four alumni from the institute who were celebrating significant birthdays: Sir Gustav Nossal and Professor Jacques Miller, who celebrated their 80th birthdays; and Professor Ian Mackay and Dr Margaret Holmes, who celebrated their 90th birthdays.

The thymus was the last organ to have its function explained. Professor Miller made the discovery whilst working at the Chester Beatty Research Institute and published his landmark study on "the immunological function of the thymus" in *The Lancet* in 1961.

Sir Gustav, Professor Miller and Professor Mackay all made seminal discoveries in the field of immunology during their time at the institute. In 1958, Sir Gustav identified that one immune cell was only able to produce one type of antibody. In the 1950s and 1960s Professor Mackay led the field of research into autoimmune diseases, coining the term 'autoimmunity'.

The event commemorated more than 140 years of service to the institute by Professors Miller and Mackay, Sir Gustav and Dr Holmes.

Their achievements were celebrated by former colleagues including Professor Michael Good, Professor Sir Marc Feldmann, Dr Graham Mitchell and Professor Mathew Vadas.

Sir Gustav, director of the institute from 1965 until his retirement in 1996, reflected that his more than 30 years at the institute got off to a 'bad start'. "I had come to work under the world's greatest virologist, Sir Macfarlane Burnet, and to my dismay he was phasing out virus work, turning the institute almost entirely towards immunology. I was disappointed at first; little did I realise that he had climbed onto a huge wave that was just about to break, propelling us younger workers into a glorious future," he said.

The four legends, (from left) Dr Margaret Holmes, Sir Gustav Nossal, Professor Jacques Miller and Professor Ian Mackay.

# Public engagement

**The institute's public engagement program has seen many hundreds of people visit the institute this year. Hundreds more have been visited by institute scientists as they take part in external programs such as CSIRO's Scientists in Schools (see page 57).**

Public lectures are one way the community can find out about work that is happening at the institute. Two public lectures were held at the institute this year, with more than 300 attendees. In December 2010, Professor Andrew Roberts shared his knowledge on blood cancers and the latest developments in treatments, while the topical issue of infectious disease and antibiotic-resistant bacteria was discussed at a panel on 'microbial wars' in March 2011.

The information shared during our discovery tours (see page 56) and public lectures is complemented by the work of the institute's biomedical animation studio, WEHI.TV. WEHI.TV continues to be a valued resource internationally for people seeking accurate scientific visualisations of biological systems and processes (see highlight, below).

This year, in addition to the work of WEHI.TV, we produced a short movie to illustrate the research and mission of the institute. The movie gained a wider audience when Qantas Airways made it part of its in-flight entertainment. The movie can be viewed on our website or YouTube channel.

The past 12 months have seen a continuation of the marked increase in media coverage on research and other activities at the institute. Several research highlights from the institute received a large amount of newspaper, TV and radio coverage including research on breast cancer, HIV, malaria, coeliac disease, type 1 diabetes and ovarian cancer. Institute scientists are increasingly being sought to provide commentary on important issues in scientific research, policy and communication.

## WEHI.TV

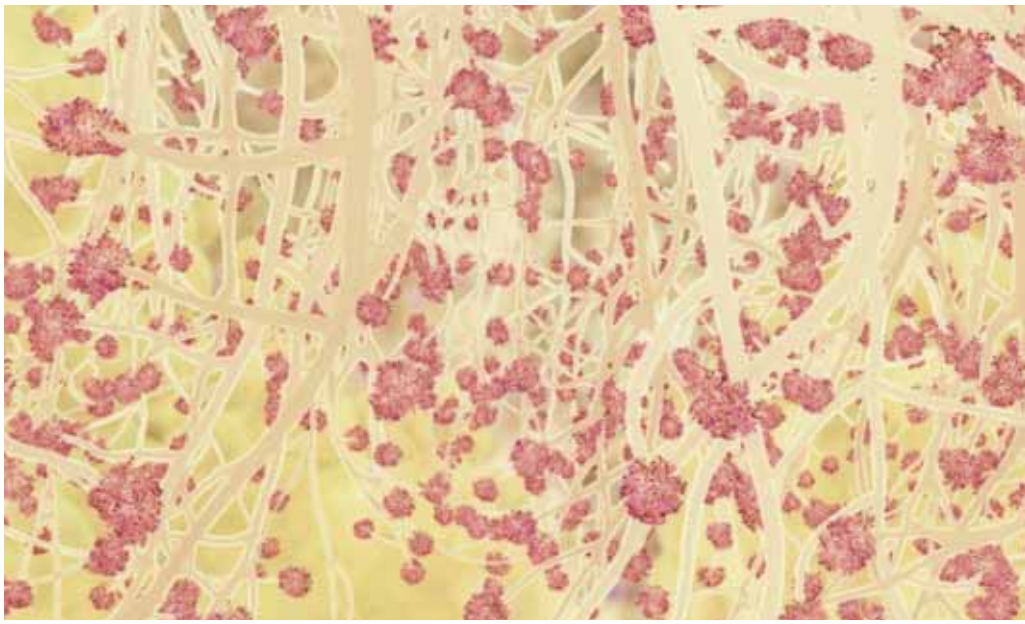
**The institute's biomedical animation studio, WEHI.TV, continues to be a valued resource internationally for people seeking accurate scientific visualisations of biological systems and processes.**

We continue to receive a large number of requests for the animations from media, science institutions, schools and students who use the videos as educational and entertainment resources. Visits to the WEHI.TV YouTube channel, WEHImovies, have risen 53 per cent in the past year.

This year, biomedical animators Mr Drew Berry and Ms Etsuko Uno created three new animations. The animations, *Breast Stem Cells, Control of Breast Stem Cells* and *Origins of Breast Cancer* depict the latest research from the institute's Stem Cells and Cancer division, and give an overview of the mammary gland, how breast stem cells are influenced by and respond to female hormones, and the role breast stem cells play in the development of some breast cancers.

This year, Mr Berry was recognised for his remarkable achievements and vivid, fascinating animations by being named one of 23 recipients of the 2010 MacArthur Fellowship. Nicknamed the 'Genius Award', the Fellowship is a prominent prize awarded to United States citizens of any age, working in any field, who "show exceptional merit and promise for continued and enhanced creativework".

A still from WEHI.TV's animation *Breast Stem Cells.*



## Discoveries Need Dollars: protecting medical research

**In 2011 medical researchers from around the country, along with colleagues in the health care sector and many members of the Australian community, united under the Discoveries Need Dollars campaign banner and fought successfully to preserve National Health and Medical Research Council (NHMRC) funding from cuts in the 2011–12 federal budget.**

The prospect of funding cuts was undeniable. The message from government was that to bring the budget back into surplus every dollar of spending was being examined and no area was to be quarantined. Many feared government sentiment was that the community did not care about medical research.

The institute initiated the Discoveries Need Dollars campaign as a voice for supporters of medical research. The community responded with:

- more than 12,000 people attending Rallies for Research in five states in April, including 4500 in Melbourne (see below);
- more than 15,000 letters and postcards to the Prime Minister, Treasurer, Health Minister, Minister for Mental Health and Ageing and myriad local members of parliament and senators;
- more than 12,000 signatures on a petition tabled in parliament by the Federal Member for Melbourne Mr Adam Bandt;
- more than 235,000 visits to the Discoveries Need Dollars website, plus strong support for the campaign's social media presence on Twitter, Facebook and LinkedIn;
- letters from Nobel Prize winners, Australians of the Year, former Premiers and other eminent members of the community;
- support from medical research bodies, individual medical research institutes, universities and hospitals, patient groups; and, most importantly,
- myriad heartbreaking and inspiring stories about ordinary Australians battling devastating disease who have benefited from medical research, either because of improved care or because it provides hope.

Minister for Mental Health and Ageing the Hon. Mark Butler MP, who has responsibility for the NHMRC and stewardship of the medical research budget, announced a review of the medical research sector following the campaign. Institute staff have coordinated the submission of comments from the Discoveries Need Dollars community on the terms of reference.

The institute's management is optimistic that this review will deliver a more efficient, better resourced medical research enterprise that reflects the passion and verve of our researchers. We are continuing to work with the organisations and individuals that supported the Discoveries Need Dollars campaign to ensure that support for medical research remains a priority area for state and federal governments, and for the broader community.


The postcards distributed during the Discoveries Need Dollars campaign.

## Melbourne rallies for research

**Supporters of medical research came out in force on the lawns of the State Library of Victoria on 12th April 2011 to protest the government's proposed cuts to NHMRC funding.**

More than 4500 people attended the rally, including staff from all major medical research centres in Melbourne and members of the wider community, many of whom were concerned about the impact of research cuts on their families' future health.

Hundreds of institute staff, many wearing white lab coats, carried signs with slogans such as 'SOS: Save our Science' and 'Survivors not Surplus'.

Protestors chanted 'Cures Not Cuts' and 'Research Saves Lives' as they waved banners and cheered MC Dr Krystal Evans, a researcher from the institute's Infection and Immunity division, in her pleas for the government to save medical research from cuts to the federal budget. Federal Member for Melbourne Mr Adam Bandt addressed the rally, as did three members of the public who were deeply concerned about the planned cuts: Ms Nerissa Mapes, who is an ambassador for, and is affected by, Parkinson's disease; Mr Sean Lusk, who has cystic fibrosis; and Ms Linda Rodger, who has lost family members to motor neurone disease.

The Melbourne Rally for Research was an astounding success, and together with rallies in seven other Australian cities, sent a strong message to the government about the high level of community support for medical research.


Federal Member for Melbourne Mr Adam Bandt (above right) with institute researchers Professor Len Harrison (above left) and Dr Margo Honeyman at the Melbourne Rally for Research.

## Governor-General visits

**In December 2010, the Walter and Eliza Hall Institute was proud to host a visit by Her Excellency, the Governor-General Ms Quentin Bryce AC.**

The Governor-General has a longstanding interest in medical research, which was enhanced when, in June 2010, she led an official delegation to Shanghai, China, that included institute scientist Dr Erika Cretney.

Dr Cretney and Her Excellency both appear in the documentary *Sisters* which screened at the Australian Pavilion at the World Expo in Shanghai. The documentary showcases the achievements of 21 women from Australia and China.

During her visit to the institute the Governor-General was briefed on recent discoveries at the institute into breast cancer, programmed cell death and epigenetics. Dr Marnie Blewitt gave an overview of her studies into epigenetics, a relatively new field of research that seeks to reveal how gene expression is controlled. Her presentation was followed by Dr Erinna Lee discussing how studies of programmed cell death could lead to new cancer treatments and Dr Samantha Oakes outlining her research into breast development and how it improves understanding of breast cancer and its treatment.

Institute director Professor Doug Hilton said it was an honour to host the Governor-General at the institute.

"The Governor-General has made clear her interest in medical research and its potential to improve human health," Professor Hilton said. "We were thrilled that she chose to visit our institute to gain a better understanding of how we are tackling the research questions that need to be answered if we are to truly bring health benefits to patients."

Institute director Professor Doug Hilton (above left) and Her Excellency Ms Quentin Bryce AC.

## Creating conversations about science

**Researchers from the Walter and Eliza Hall Institute are committed to discussing and reporting on their scientific discoveries to encourage greater understanding of science and the scientific process.**

In July 2010, coeliac disease researcher Dr Bob Anderson revealed that he and his colleagues had identified the three key proteins in gluten that were toxic for people with coeliac disease. Dr Anderson said it had been 60 years since gluten was discovered to be the environmental cause coeliac disease.

"In the years since, the holy grail in coeliac disease research has been to identify the toxic peptide components of gluten; and that's what we've done," Dr Anderson said.

The discovery attracted significant media attention. In this photo, Dr Anderson is talking to TV news crews about the finding, in a press conference held at the institute.

## Discovery tours

**The institute's discovery tour program has received a phenomenal public response this year.**

Almost 700 people from 30 groups attended our discovery tours where they found out about the research underway at the institute. Our researchers volunteer their time to take attendees on a tour of their laboratories and share their latest research findings and insights into disease and human health.

During the year, scientists presented their research findings on breast stem cells and their role in breast cancer, the lifecycle of platelets and how this information may be useful in developing blood products with a longer shelf-life, new research into 'pro-survival' proteins that are important in the development of blood cancers, and boosting the immune system as a means of treating chronic virus infections.

Privately organised tours throughout the year included visits from school groups, Probus groups, golf clubs, private organisations, other research institutes, hospitals and universities. Some of the groups that attended tours this year included the Australian Cancer Research Foundation, Berwick Ladies Probus, Ivanhoe Grammar School, McKinnon Secondary College, Redcliffs Secondary College Mildura, Nanyang Polytechnic University, Singapore, Rotary Club of Eltham, Royal Women's Hospital senior management group, and University High School teachers.

Brigitte, a student from McKinnon Secondary College, said she'd had a great experience at the institute. "It's so interesting, I think it's such a great experience just to see the amazing job [the researchers] are trying to do to," she said. "All the research into immunology and disease, it's just mind-blowing."

# Engagement with schools

**The institute is a strong advocate for science education and engages with school students to promote a vibrant science curriculum that will inspire the next generation of potential scientists. Public speaking commitments by institute staff and students in schools and in the community increased by 22 per cent in 2010-11.**

Many of our staff and students volunteer their time to participate in engagement activities in schools. Our students volunteer at the Gene Technology Access Centre, where they develop and run experiments for secondary school students. Researchers also visit schools to speak about their research. Our scientists are active in advocating for gender equity in health and medical research. They have visited a number of schools this year to talk to school students about careers for women in science. This year some of the schools our scientists visited were Brunswick Early Learning Centre, Carey Baptist Grammar School, Castlemaine North Primary School, Malvern Primary School, Northcote High School, Preston Girls Secondary College and Scotch College.

A number of our scientists are involved in the CSIRO's Scientists in Schools program, which fosters long-term partnerships between teachers and scientists to provide inspiration and ideas for science learning in schools. They are also recruited to participate in organised programs such as 'Speed Science', the National Youth Science Forum and *I'm a Scientist, Get me out of here!*

## GTAC: the Gene Technology Access Centre

**GTAC is a collaboration between the Walter and Eliza Hall Institute, the Department of Microbiology and Immunology at The University of Melbourne and University High School.**

The past year has seen more than 6000 school students accessing GTAC's programs, including off-site visits to primary schools. In 2011 GTAC hosted two immunology-themed programs combining laboratory activities with seminars from scientists including Sir Gustav Nossal and Nobel Laureate Professor Peter Doherty. Other highlights have been the annual teacher symposium on the role of chemistry in biological research, and the participation of the Victorian Minister for Education, Mr Martin Dixon, in the 'Genetech' laboratory program during Education Week.

Mr Brian Stevenson, outgoing director of GTAC, said the centre provided an exemplar model for the establishment of other specialist science centres. "It has been a privilege to allow so many students and teachers from all educational sectors across Victoria to access some of the country's brightest young scientists and eminent researchers through programs that reflect the contemporary nature of bioscience," he said.

A junior participant in DNA Fun Sunday held at GTAC during National Science Week.

## I'm a Scientist, Get me out of Here!

**In June 2011 Dr Krystal Evans from the Infection and Immunity division competed in the Australian pilot of *I'm a Scientist, Get me out of here!*, a federal government-funded science enrichment and engagement program.**

*I'm a Scientist, Get me out of here!* involved 15 young Australian scientists who spent up to two weeks online fielding questions from 1500 students at 34 Australian schools, and participating in online discussions with science classes. In the second week of the competition students voted for their favourite participant in each of three 'zones' based on the scientists' interest areas of health, food or general science.

Dr Evans was one of five scientists who competed in the Health Zone, answering questions on topics such as 'are viruses alive?', 'what's your biggest career goal?' and 'how important do you think your research is?'

Dr Evans said the event sharpened her communication skills. "It was great to get some insight into how research is perceived and understood by school students and what scientific issues concern them about the future," she said.

It is anticipated that *I'm a Scientist, Get me out of here!* will be an annual program.

# Donor and bequestor engagement

**The support of donors and bequestors means a great deal to our scientists and directly advances the institute's research program. This year marked the establishment of a new program to acknowledge and thank our donors and bequestors for their loyal support of the institute.**

In 2011, institute director Professor Doug Hilton initiated a series of research briefings for long-standing donors, some of whom had supported the institute for more than 35 years and were visiting the institute for the first time.

Professor Hilton also invited individuals who had notified the institute that they had made a gift in their will to join him for updates on recent research initiatives and on developments in the medical research sector.

During these presentations, Professor Hilton acknowledged the significant contribution of donors and bequestors to the establishment and development of the Walter and Eliza Hall Institute over the past 96 years, and the importance of this support for the institute's research.

We were pleased to hear that guests enjoyed the research briefings, in particular learning more about what the institute is doing and meeting other donors and bequestors. This feedback has seen the institute commit to continuing this program in 2012.


In May, bequestors joined deputy director Professor David Vaux (centre) for a laboratory tour followed by lunch hosted by director Professor Doug Hilton, who gave an update on institute research initiatives and on developments in the medical research sector.

## Supporting research into childhood diseases

**In December 2009, the late Mrs Paddy Pearl auctioned her home, Campania House, in Tasmania. Mrs Pearl kindly donated some of the proceeds to the institute, which were used to establish a PhD scholarship to support research into diseases that affect children.**

To show appreciation for Mrs Pearl's support, institute director Professor Doug Hilton visited her at Saint Canice Lifestyle Village in Sandy Bay, Tasmania, to thank her for her generous donation and formally announce the $100,000 Cyril and Paddy Pearl Scholarship.

Professor Hilton was accompanied by breast cancer researcher Dr Sam Oakes, general manager Ms Maureen O'Keefe and head of fundraising Ms Deb Cutts. The group met with 70 residents of Saint Canice and Dr Oakes gave a presentation on the latest developments in the institute's breast cancer research program.

Professor Hilton said he treasured the opportunity to meet with Mrs Pearl and thank her personally for making it possible to establish the Cyril and Paddy Pearl PhD Scholarship.

"Paddy Pearl's philanthropy and belief in what we are trying to achieve as an institute has given our researchers tremendous encouragement. Her personal commitment to improving the quality of life and health outcomes for her fellow Australians and people around the world is an inspiration," he said.

"Our scientists are working to find causes, methods of prevention and treatments for several diseases that have a huge impact on children, including leukaemia, rheumatic fever, malaria and type 1 diabetes."

The Cyril and Paddy Pearl Scholarship was awarded to PhD student Mr Alan Yap from the institute's Infection and Immunity division. Mr Yap is studying malaria, primarily a disease of children under five years of age and one of the biggest paediatric killers worldwide.

# Sustainability

The exterior of the renovated Walter and Eliza Hall Institute building in Parkville, Melbourne.

# The Board

## The directors of the Walter and Eliza Hall Institute of Medical Research board

### Mr Leon A Davis AO Dip Prim Metallurgy *SAIT* Hon DSc *Curtin* Hon DSc *Qld* Hon DUniv *UniSA* FRACI FAIMM

**President**

Appointed: **February 2001**
Term expires: **May 2013**

Mr Davis became chief executive of Rio Tinto Ltd and Rio Tinto plc on 1 January 1997 and retired from the position in 2000. Previously he had been deputy chief executive and chief operating officer of RTZ-CRA.

Mr Davis joined the CRA Group in 1956 as a metallurgical cadet. In 1989 he was appointed a group executive of CRA Limited. Until joining RTZ in 1991 as mining director, his appointments included chairman of Argyle Diamond Mines, Dampier Salt, Wimmera Industrial Minerals and Kalimantan Gold.

In December 2000 Mr Davis became chairman of Westpac Banking Corporation, stepping down from the position in 2007.

### Mr Steven M Skala AO BA LLB (Hons) *Qld* BCL *Oxon*

**Vice-President**

Appointed: **June 1999**
Term Expires: **June 2014**

Mr Skala is vice chairman Australia & New Zealand of Deutsche Bank AG and a former senior partner of Arnold Bloch Leibler lawyers.

He is chairman of Wilson HTM Investment Group Ltd and a director of the Australian Broadcasting Corporation and Hexima Limited. He is deputy chairman of The General Sir John Monash Foundation, a director of the Centre for Independent Studies and a member of the International Council of New York's Museum of Modern Art.

Mr Skala is a member of the advisory council of the Australian Innovation Research Centre, the Global Foundation and the Grievance Tribunal of Cricket Australia. He is the immediate past Chairman of Film Australia Limited and the Australian Centre for Contemporary Art.

### Mr Roger E Male LLB *Adelaide* Dip Acctg *Swinburne*

**Honorary Treasurer**

Appointed: **June 1998**
Term Expires: **May 2013**

Mr Male was a partner of Coopers & Lybrand for more than 20 years and retired from the firm as a member of its national committee and Melbourne office managing partner in 1998.

He is a director of Goldman Sachs Management and Partners Ltd, and the Uniting Church Funds Management Ltd.

Mr Male is also a member of the Almond Orchards Limited compliance committee and the Nillumbik Shire Council audit advisory committee.

## Professor James Angus AO BSc *Syd* PhD *Syd* FAA

Appointed: **November 2003**
Term expires: **at discretion of The University of Melbourne**

Professor Angus is dean of the Faculty of Medicine, Dentistry and Health Sciences at The University of Melbourne. He was president of the university's academic board and has served on the university's council as well as the council of the Australian Academy of Science.

He currently serves on the boards of Melbourne Health, the Mental Health Research Institute, the Victorian Institute of Forensic Medicine, and the Victorian Comprehensive Cancer Centre. He is past president of Medical Deans Australia and New Zealand, and is honorary secretary to the Victorian Rhodes Scholarship Committee. Professor Angus was awarded the Gottschalk Medal in 1984, the Centenary Medal in 2003 and the Australian Citation Laureate Award for Pharmacology in 2004. He was appointed Officer of the Order of Australia in June 2010.

## Mr Mike C Fitzpatrick BA (Hons) *Oxon* BEng (Hons) *UWA*

Appointed: **February 2001**
Term Expires: **February 2013**

Mr Fitzpatrick is chairman of the Australian Football League, Treasury Group Limited, Infrastructure Capital Group, and a non-executive director of Rio Tinto plc.

He is the founder and former managing director of Hastings Funds Management Limited. In that role, Mr Fitzpatrick was a director of a number of Hastings-managed investments including Pacific Hydro Limited, Global Renewables Limited, Utilities of Australia, Australian Infrastructure Fund and Airstralia Development Group Pty Ltd (Perth Airport).

Mr Fitzpatrick was a premiership captain (1981, 1982) with the Carlton Football Club in the Australian Football League and a first-grade cricketer. He was formerly a member of the Melbourne Park Tennis Centre Trust, a director of the Carlton Football Club, chairman of the Australian Sports Commission and, in the early 1980s, vice-president of the AFL Players' Association.

## Professor Jim McCluskey BMedSc MB BS MD *UWA* FRACP FRCPA

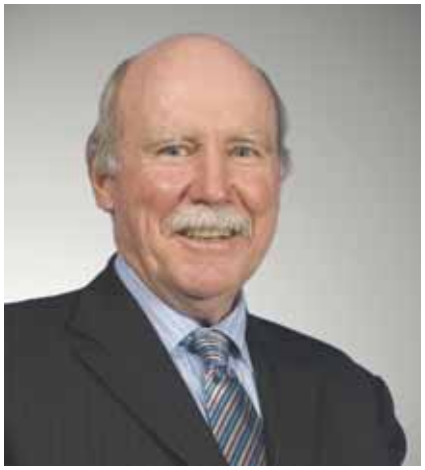
Appointed: **April 2011**
Term expires: **at discretion of The University of Melbourne**

Professor Jim McCluskey became the deputy vice-chancellor (research) at The University of Melbourne in March 2011. Prior to this he was the pro vice-chancellor (research partnerships), chair of Microbiology and Immunology and deputy head of that department.

Professor McCluskey has an international reputation for his research in basic and clinical immunology. He has consulted for the Australian Red Cross for more than 20 years and is editor-in-chief of the international immunogenetics journal *Tissue Antigens*.

He is a member of the board of directors of the Florey Neurosciences Institute, Bionics Institute and a member of the Nossal Institute for Global Health.

Professor McCluskey replaced Professor Peter Rathjen as The University of Melbourne's representative on the institute board in March 2011.



## **Dr Graham F Mitchell** AO RDA BVSc *Syd* FACVSc PhD *Melb* FTSE FAA

Appointed: **July 2007**
Term Expires: **June 2013**

Dr Mitchell has detailed knowledge of the academia-industry interface and completed his PhD at the Walter and Eliza Hall Institute in the late 1960s. In 1973, after postdoctoral experience in the US, UK and Switzerland, Dr Mitchell returned to the institute and established a program on the immunology of parasitism.

In 1990, Dr Mitchell was appointed director of the Royal Melbourne Zoological Gardens but returned to biomedical research in 1993 as director of research in the R&D division of CSL Limited. Dr Mitchell is an adviser on innovation to the Victorian, Tasmanian, Northern Territory and Federal Governments and jointly acts as chief scientist for the Victorian Government departments of Primary Industries and Sustainability and Environment. He is a non-executive director of Antisense Therapeutics Limited, Compumedics Limited, AgVic Services Pty Ltd, Adelaide Research and Innovation Pty Ltd and Avipep Pty Ltd.

## **Mrs Linda B Nicholls** AO BA(Econ) *Cornell* MBA *Harvard* Hon FAICD

Appointed: **February 2001**
Term Expires: **February 2013**

Mrs Nicholls is a corporate adviser and a director of a number of leading Australian companies and organisations. She is chairman of KDR (Yarra Trams), and a director of Sigma Pharmaceutical Group, Fairfax Media, and the Australian Institute of Company Directors. Previously she was chairman of Healthscope and Australia Post, and a director of St George Bank. Mrs Nicholls is also vice-president and a member of the Harvard Business School Alumni board. She runs her own corporate advisory practice specialising in business strategy in financial services and health care. Mrs Nicholls has more than 30 years experience as a senior executive and company director in Australia, New Zealand and the United States.

## **Ms Kate J Redwood** BA BSW (Hons) *Monash*

Appointed: **August 2009**
Term Expires: **August 2012**

Ms Redwood has held a number of senior management positions including CEO of the Australian Physiotherapy Association, executive director of Australian Red Cross Victoria, and executive director of the Victorian Council of Social Service.

A former councillor for the City of Melbourne, Ms Redwood has chaired a number of standing committees as well as the Yarra/Melbourne Regional Library Board, the Melbourne Disability Advisory Committee and for many years was president of the Carlton Senior Citizens' Centre.

Ms Redwood is a member of the Melbourne Health board and chairs the Melbourne Health community advisory committee. In 2010, she became a director of Hepburn Wind. Ms Redwood was awarded the Centenary Medal in 2001 for services to local government and the community.

## Mr Christopher W Thomas BCom (Hons) MBA *Melb* FAICD

Appointed: **February 2001**
Term Expires: **February 2013**

Mr Thomas joined executive search firm Egon Zehnder International in 1979 and was managing partner of the Melbourne office from 1986 to 2003. He was also leader of the firm's global Board Consulting Practice Group (1998–2006) and chaired the firm's twice-yearly international partners' meetings from 1997 to 2007.

Mr Thomas is a fellow of the Australian Institute of Company Directors and the Australian Institute of Management. He has served on the board of the Corps of Commissionaires (Victoria) and the council of the Australian Film, Television and Radio School. He was a board member of the Heide Museum of Modern Art for nine years (and its chairman for three years), chairman of the Victorian Community Foundation and president of the Melbourne Business School Alumni.

## Ms Catherine M Walter AM LLB (Hons) LLM MBA *Melb* FAICD

Appointed: **February 2001**
Term Expires: **February 2013**

Ms Walter is a non-executive director of Australian Foundation Investment Company, the Reserve Bank's Payment Systems Board, Victorian Funds Management and Victorian Opera and chairman of the Australian Synchrotron.

She practised law for 20 years as a commercial lawyer, which included a term as managing partner of Clayton Utz in Melbourne. Ms Walter is a former commissioner of the City of Melbourne.

In 2003, Ms Walter was appointed a Member of the Order of Australia for her service to business, particularly as a director of a number of public companies, to the arts, to the law, and to the community through the City of Melbourne. She was awarded a Centenary Medal in the same year.

## Professor Ingrid Winship MB ChB MD *Cape Town* FRACP FACD

Appointed: **June 2007**
Term Expires: **June 2013**

Professor Ingrid Winship is the inaugural chair of adult clinical genetics at The University of Melbourne and executive director of research for Melbourne Health.

A medical graduate of the University of Cape Town, she completed postgraduate training in genetics and dermatology. In 1994, Professor Winship took up an academic position at the University of Auckland and later became Professor of Clinical Genetics and associate dean for research in the Faculty of Medicine and Health Sciences.

Professor Winship is a member of the Victorian Cancer Action Plan implementation committee, NHMRC Human Genetic Advisory Committee, Victorian Life Sciences Computation Initiative steering committee and the Australian Synchrotron clinical advisory panel.

# General manager's report

## Building redevelopment

Over the past financial year a significant milestone was reached with the handover of the institute's new west wing, which was completed in December 2010. The project was achieved on time and on budget, producing a first-class building of which the institute and its wider community are very proud. Refurbishment of the east wing is now underway and will continue into 2012, resulting in a fully-integrated $185 million research facility. The success of the project to date has been made possible by the strong partnerships that were developed early between the institute and the architects (Denton Corker Marshall and S2F), the builders (Baulderstone's BPL) and the consultant team (Aurecon, Donald Cant Watts Corke and others).

## Financial sustainability

Relationship building also underpins the institute's approach to raising funds for research. We are focused on getting to know our supporters and their needs, whether they are individual donors, trusts and foundations, corporations or government. Over the past year many of these supporters played a pivotal role in supporting the institute-initiated Discoveries Need Dollars campaign. As a result of this national campaign and everyone's combined efforts, the campaign was successful and government cuts to medical research funding did not eventuate. However, there was also no significant increase in medical research funding, at a time when there are four applications for every one project grant awarded by the National Health and Medical Research Council (NHMRC).

Despite the ongoing intense competition for research grants, institute scientists have continued to be successful in obtaining competitive grant funding. Our success rate for project grants awarded through the NHMRC was again amongst the highest in Australia, with slightly more than 50 per cent of our applications funded. In addition, two of our largest NHMRC program grants were renewed.

On the international stage, we were awarded a National Institutes of Health (US) Creative and Novel Ideas in HIV Research grant; one of our Grand Challenges Explorations grants, administered by the Bill & Melinda Gates Foundation, successfully progressed to stage 2 funding; and we were awarded two Human Frontier Science Program collaborative grants.

Three institute laboratory heads attracted new fellowships, with two NHMRC senior research fellowships and a senior medical research fellowship from the Sylvia and Charles Viertel Charitable Foundation being awarded.

While fighting budget cuts, applying for grants and raising funds for research throughout the year, the institute has been furthering its continuous improvement strategy of keeping costs low and improving operational efficiency to ensure that every dollar raised, whether from competitive peer-reviewed grants, or philanthropic, corporate or government donations and grants, goes as far as possible, thereby ensuring the institute's long-term financial sustainability. This includes funds received from the Victorian Government (under the Operational Infrastructure Scheme) and the Australian Government (under the Independent Research Institutes Infrastructure Support Scheme) for the indirect costs of research. Contributions received through these schemes are desperately needed by the institute to fund the infrastructure and operations that support the research. The institute is advocating for a simple transparent system where every dollar received for direct research costs is supplemented by 60 cents from government for indirect costs. This is in place of the current complex multi-tiered system which only provides 28 cents in each research dollar for indirect costs.

During the year the institute has reduced costs and improved efficiencies by:

- renegotiating contracts for insurance, cleaning, gas and electricity;
- entering into a collaborative agreement with The University of Melbourne for access to library services;
- consolidating waste management under a broader shared operating agreement with Melbourne Health;
- outsourcing courier services;
- redesigning service delivery models for information technology, bioservices, imaging and media production;
- carrying out a store tender process;
- reviewing costing and charging models for scientific services;
- making progress towards reducing leave liabilities;
- introducing online compliance training;
- enhancing human resources and finance information systems; and
- implementing an electronic document management system.

The general manager's advisory group: back row (from left), Mr Steve Droste, Dr John Wastell, Ms Deb Cutts, Ms Maureen O'Keefe, Mr Paul Fraser, Mr Murray Jeffs, Mr Stanley Balbata; front row, Ms Penny Fannin, Dr Julie Mercer, Dr Helene Martin, Dr Catheryn O'Brien, Mr Michael Rubira, Ms Josephine Marshall.

## Research technology and services

The institute's newly-established Scientific Services Committee and Senior Technology Planning Group have already played an important role in assessing our current and future scientific services and technology needs. We have formed technology partnerships with equipment suppliers by becoming a reference or pilot site in the areas of imaging, proteomics and flow cytometry. Further, equipment sharing has been made possible through academic collaborations with the Bio21 Institute, the Peter MacCallum Cancer Centre and the Victorian Comprehensive Cancer Centre, among others.

During the year a major restructure of the proteomics facility, led by the new head of the Systems Biology and Personalised Medicine division, Professor Liam O'Connor, was completed. This involved ending our joint agreement with the Ludwig Institute for Cancer Research (LICR) and the Walter and Eliza Hall Institute taking full responsibility for proteomics and the operations and personnel relating to proteomic experiments. A mixed collaborative research and service model has been developed and the facility will operate as a reference site for advanced proteomics instrumentation. This will give our researchers and our external clients access to the latest mass spectrometric and bioinformatic analysis techniques.

## Planning, legal, compliance and risk

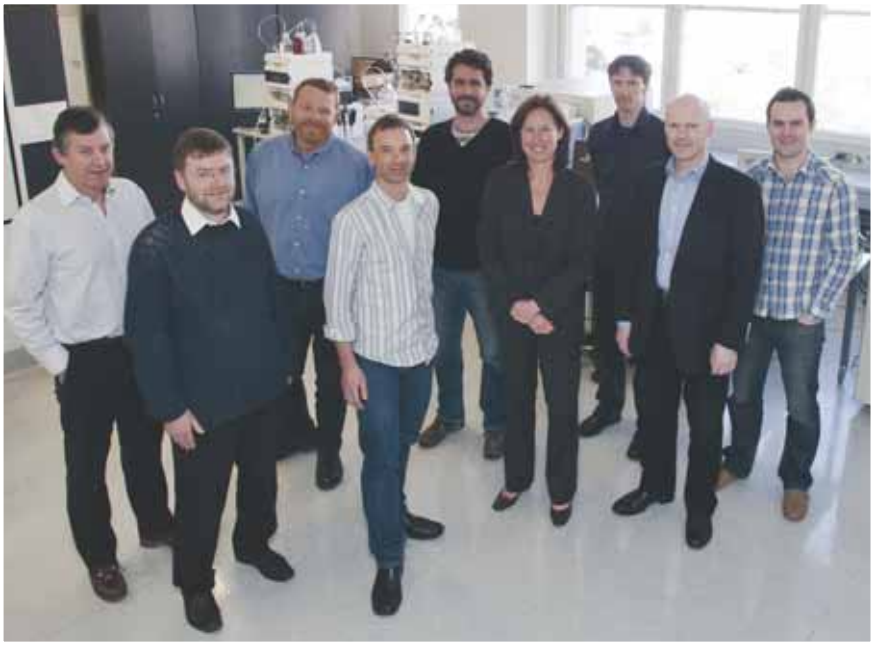
The institute's new planning documents, including the 2010-2015 Strategic and Operational Plans and budget have come to the end of their first year and a report of progress against key strategic performance indicators has been prepared for the board. Each year the plans will be reviewed as part of the annual planning and budget cycle to ensure they are current and relevant.

During the year lease negotiations successfully resulted in new leases with favourable terms for the institute's proteomics facility and Systems Biology and Personalised Medicine division in buildings adjacent to the institute. The lease for our new, expanded institute has been agreed for 99 years less one day for peppercorn rent, and is awaiting signature by the Victorian health minister.

During the year the institute's key compliance committees: Human Research Ethics, Animal Ethics, Safety, and Biosafety, all met regularly. Reports were provided to the board and/or senior management as required.

The institute risk management strategy and crisis management plans continue to be reviewed. The risk plan for the institute's building expansion project has been reviewed and revised as the project moves from the main works to the remaining works construction phase.

As part of an ongoing program of rolling audits approved by the Audit and Risk Committee, the following audits were conducted during the year: fundraising, travel, salary expenditure, scientific services cost recovery, procurement and health and safety.



The institute and LICR team behind the move of the proteomics facility to the institute (from left): Mr Michael Rubira, Mr Simon Michnowicz, Professor Liam O'Connor, Dr Thomas Nebl, Mr Giuseppe Infusini, Ms Maureen O'Keefe, Mr Grant Thomas, Dr John Wastell, Dr Andrew Webb.


The new signage on the eastern wing of the institute.

# Building our future

## Towards gender equity in medical research

**For decades the medical research sector has observed that women, who make up more than 50 per cent of its undergraduate and PhD students, are seriously under-represented at senior levels.**

This has been attributed to the difficulties faced by women in making the transition from postdoctoral scientist to laboratory head and, from there, to more senior roles.

To address these issues at the institute a Gender Equity Committee (GEC) was formed in February 2010 to plan, facilitate and administer gender equity initiatives. The GEC is co-chaired by Associate Professor Lynn Corcoran and Professor Terry Speed and its members represent a cross-section of the institute staff.

This year, the institute appointed four new female laboratory heads, increasing the percentage of senior female researchers to 24 per cent from 21 per cent in 2009-10. The institute is a signatory to the United Nation's women's empowerment principles.

This year, the GEC undertook a number of initiatives to improve facilities available at, and through, the institute. These included:

- installing a family-friendly lecture viewing room at all conferences held at the Mantra Erskine Beach Resort at Lorne, Victoria, allowing parents to participate in the conference while caring for their children;
- making institute-sponsored access to childcare and associated services available for staff; and
- continuing the childcare subsidy, which provides senior female researchers with up to $15,000 a year towards the cost of care for pre-school-age children. Currently, six laboratory heads and senior postdoctoral researchers are receiving this subsidy.

A staff survey was undertaken this year to help us understand the issues faced by researchers in their career development at the institute. Feedback highlighted a number of issues, particularly for postdoctoral level scientists as they face the transition to laboratory head, often during their childbearing years. Further, more focused, surveys are planned for 2011 and beyond to continue to explore these issues.

The institute and the GEC also participated in and sponsored several forums on equal opportunity and women in research, including:

- WiSE (Women in Science and Engineering) Summit, 11 April 2011, Canberra;
- Gender Equity Workshop, 17 June 2011, Melbourne.

Institute director Professor Doug Hilton welcomes attendees to the Gender Equity Workshop, held in June 2011.

## Financial Sustainability Committee

**Sustainability is one of the five pillars of the institute's Strategic Plan. One of the goals of this pillar is for the institute to gain independence from government funding cycles. This is crucial if we are to recruit the scientists, purchase the technologies and undertake the bold experiments that will allow the institute to thrive into the future.**

To help meet this objective a board sub-committee, the Financial Sustainability Committee, was established in March 2011. The committee is chaired by board member Mr Chris Thomas.

Joining Mr Thomas on the committee are people with complementary skills and experience in industry superannuation, venture capital, law, marketing and advertising and banking and finance.

The committee is supporting and enhancing institute activities aimed at securing our financial future and is a welcome addition to our structure.

Some of the Financial Sustainability Committee members, from left to right: Ms Deb Cutts, Mr Rowan Kennedy, Mr Michael Daddo, Mr Chris Thomas (chair), Professor Doug Hilton, Ms Caroline Johnston, Ms Maureen O'Keefe.

## Building redevelopment

**Since 2009, the institute has been undergoing a significant building redevelopment to almost double the size and research capacity of the institute. The redevelopment has largely been made possible through the generosity of the Australian and Victorian governments and The Atlantic Philanthropies.**

On 16 December 2010, the keys to the new west wing of the building were handed over and we started the task of moving the equipment and people of dozens of laboratories into the new building. The west wing houses seven levels of laboratories and scientific support services as well as an insectary to enable malaria researchers to target the critical liver stage of the malaria life cycle, and advanced cell and tissue imaging and flow cytometry centres.

The building redevelopment moved into the next stage in early 2011, with the refurbishment of the existing building now in full swing.

The new laboratories in the west wing of the institute. The new wing has been designed such that there are separate areas for offices and laboratories.

## Institute donor for 46 years, Mr Eddie Brownstein

**As an undergraduate medical student in Johannesburg in the 1950s, Mr Eddie Brownstein was confronted daily by the impact of apartheid on the community. "The black community had very poor living conditions, very poor salaries and vast amounts of crime," he said. "You saw that people couldn't sustain life, they couldn't sustain their children."**

Mr Brownstein says that when women came into the clinic with their children, covered in rashes, septic and dying, the doctors would ask what had happened. "'*Daar is niks geld baas*' [there is no money boss]. We heard that so often."

Mr Brownstein and his medical student colleagues decided to do something. "We decided to donate funds to support a new program initiated by the Anglican church to feed black children in primary schools. That was the beginning for me; when I saw poverty and decided I must do something," he said.

A graduate in medicine from Witwatersrand University, Johannesburg, Mr Brownstein trained in general surgery in Scotland and England. In 1961, after the Sharpeville massacre in South Africa, he and his wife, with their two young sons, decided to migrate to Australia. For the next 25 years, Mr Brownstein worked as a general surgeon in public and private practice at the Wimmera Base Hospital in Horsham, Victoria.

"For the first seven years I was on call 24 hours a day for surgical problems," Mr Brownstein said. "These were the days before seat belts and with lots of speeding cars."

In 1965, following the death of his father, a stockbroker, Mr Brownstein suddenly found he had the funds to be able to do more. "I took leave from work because I had to do some thinking, and you can't think enough when you are working," he said.

After seeking advice from lawyers, Mr Brownstein decided to establish a philanthropic trust to improve the lives of people needing care. He then heard about a new director appointed at the Walter and Eliza Hall Institute, Gus Nossal, and asked if he could have a meeting.

"It was Gus who put me in the right direction," Mr Brownstein said. "He discussed the institute's research with me, he introduced me to talented researchers and I decided then to donate to the institute's cancer research."

Mr Brownstein's support of the institute now spans 46 years and includes recent significant support for building works and construction. He also served for 11 years as a member of the institute's Human Research Ethics Committee after being approached by Professor David Vaux.

"David suggested that my studies in bioethics and background experience made me a good candidate," he said. "I was honoured that David recommended me as a committee member."

When asked what drives his wish to donate, Mr Brownstein contemplated the question for some time. "Compassion," he said. "It's not religion, not justice and rules, or even individuals that drive me, but compassion."

Mr Eddie Brownstein, pictured below right with deputy director Professor David Vaux, has supported the institute for 46 years.

# Institute organisation

# Members of the institute 30 June 2011

The University of Melbourne
The Royal Melbourne Hospital
Dr Susan Alberti AO
Professor James A Angus AO
Mr Donald Argus AC
Sir James Balderstone AC
Mrs Ann D Bates
Mr Robert Bates
Mr Lance H J Bauer
Mr Marc Besen AO
Dr Peter Brennan
Mrs Beverley A Brownstein
Mr Edward G Brownstein
Dr Margaret N Brumby AM
Professor Tony Burgess AC
Professor Christopher J Burrell AO
Professor Robert Burton
Dr David Campbell
Mr Terrence A Campbell AO
Professor David E Caro AO OBE
(dec. 15 August 2011)
Mr Alan J Chatterton AM
(Trustee of the Walter and Eliza Hall Trust)
Lady Susannah Clarke
Professor Gordon Clunie
The Rt Hon Sir Zelman Cowen
Mr John F Cowper
(Trustee of the Walter and Eliza Hall Trust)
Mr John Dahlsen
Mr Stephen Daley
Mr Leon Davis AO
Mrs Annette Davis
Professor David de Kretser AC
Mrs Helen M Diamond
Mr Ronald F Diamond
Ms Melda K Donnelly
Professor Ashley R Dunn
Mr John W Dyson
Dr Peter P-H Eng
Mr Robert Evans
Mr Mike C Fitzpatrick
Professor Richard Fox AM
Professor Alan D Gilbert AO
(dec. 27 July 2010)
Professor James Goding
Mr John B Gough AO OBE
Associate Professor Nicholas M Gough
Mr John L Greig
Sir Andrew Grimwade CBE
Mrs Anne Grindrod
Mrs Jean T Hadges
Dr Emanuela Handman
Mr Harry M Hearn AM
Dr Margaret C Holmes
Dr Thomas H Hurley AO OBE
Mr Darvell Hutchinson AM
Ms Helen Kennan
Mr Warwick G Kent AO
(Trustee of the Walter and Eliza Hall Trust)
Professor Emeritus Priscilla S Kincaid-Smith AC OBE
Professor Frank Larkins AM
Professor Richard Larkins AO
Mr Gary W Liddell
Professor Emeritus Athol W J Lykke
Professor Emeritus Ian R Mackay AM
Mrs Avis L Macphee AM
Ms Eve Mahlab AO
Mrs Robyn G Male
Mr Roger Male
Professor Ray Martin AO
Professor Emeritus Thomas J Martin AO
Mr Erich A Mayer AM
Dr Neville J McCarthy AO
Mrs Jean M McCaughey AO
Professor Jim McCluskey
Professor John A McKenzie AM
Professor Frederick Mendelsohn AO
Professor Emeritus Jacques Miller AC
Mr Robert C Minter
(Trustee of the Walter and Eliza Hall Trust)
Professor Christina Mitchell
Dr Graham F Mitchell AO
Dr Judith A Mitchell
Mr Hugh Morgan AC
Dr George Morstyn
Dame Elisabeth Murdoch AC DBE
Mr Anthony Murphy
Ms Linda Nicholls AO
Lady Lyn Nossal
Mr Tom O'Brien AM
Mrs Marion Page
Sir Arvi Parbo AC
Mrs Paddy Pearl
(dec. 8 September 2011)
Professor Roger Pepperell
Mr David Percival
Professor Emeritus Jim Pittard AM
Lady Primrose Potter AC
Mr John B Prescott AC
Professor Peter D Rathjen
Ms Kate J Redwood
Mr John B Reid AO
Mr Michael Robinson AO
Mrs Margaret S Ross AM
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Ms Linda M Sorrell
Miss Ann A Sprague
Dr John Stocker AO
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Mr Bruce B Teele
Mrs Cheryl F Thomas
Mr Christopher Thomas
Mr John Walker QC
Mr Stanley Wallis AC
Ms Catherine Walter AM
Mr John M Walter
Mr John C Warburton
Mr Robert Warren
Ms Marion J Webster OAM
Mr Kevin J Weight
Professor Richard Wettenhall
Dr Senga Whittingham
Mr David A Williamson
Professor Robert Williamson AO
Professor Ingrid Winship
Mr Peter Worcester
Mr Robert Wylie

# Supporters and donors

**The support the institute receives from government, private donors, trusts, foundations and industry is vital to achieving our strategic goals and making the discoveries necessary to advance the understanding, prevention and treatment of disease.**

We are grateful for the trust our supporters have awarded us and are committed to honouring that trust.

## Government support

**The institute is thankful for the support of the Victorian and Australian Governments.**

This year we received $31.6 million in grants and $8 million in fellowships through the National Health and Medical Research Council. A further $293,000 in grants and $1.58 million in fellowships was received. Further support was received from the Australian Stem Cell Centre, the Australian Phenomics Facility, the Australian Department of Innovation, Industry, Science and Research, the Cancer Therapeutics Cooperative Research Centre (CTx CRC) and the HEARing Cooperative Research Centre.

The Victorian Government provided $6.8 million of support through the Victorian Breast Cancer Research Consortium, Victorian Cancer Agency, Victorian Endowment for Science, Knowledge and Innovation, Victorian Neurotrauma Initiative and the Operational Infrastructure Support scheme.

## Trusts and Foundations

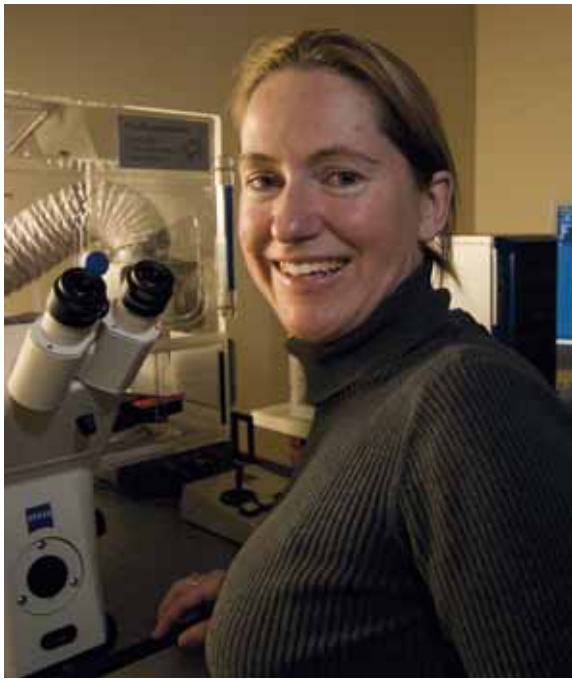
**Trusts and foundations provide crucial financial support to the institute in its pursuit of new and bold research.**

It is with this support that we are able to strengthen collaborative arrangements and programs with other research centres, address capital requirements, and produce internationally-competitive research.

We thank the following trusts and foundations that have supported our applications for funding over the past 12 months: Arthritis Foundation of Australia, Harold and Cora Brennen Charitable Fund, Cancer Council Victoria, Cure Cancer Australia Foundation, Diabetes Australia Research Trust, Thomas William Francis & Violet Coles Trust, The Bill & Melinda Gates Foundation, Juvenile Diabetes Research Foundation, Leukaemia Foundation of Australia, Leukaemia Foundation of Queensland, Harold Mitchell Foundation, Multiple Myeloma Research Foundation, National Breast Cancer Foundation, National Heart Foundation of Australia, Prostate Cancer Foundation of Australia, Ramaciotti Foundations, The William Angliss (Victoria) Charitable Fund, The Jack Brockhoff Foundation, The William Buckland Foundation, The CASS Foundation Limited, The Rebecca L Cooper Medical Research Foundation, The Dyson Bequest, The Leukemia & Lymphoma Society of America, The J.H.A. Munro Foundation Limited, The Lady Tata Memorial Trust, The Sylvia and Charles Viertel Charitable Foundation, and Joe White Bequest.

Dr Matthew Call (below left) was awarded a Victorian Endowment for Science, Knowledge and Innovation (VESKI) fellowship to continue his work at the institute.

Dr Kelly Rogers (below right) received funding from the Harold and Cora Brennen Charitable Fund for the institute's Imaging Facility.



## The Isabel and John Gilbertson Charitable Trust

**During their lives, Isabel and John Gilbertson tried wherever possible to assist those in need, as well as support and encourage community projects that strive to relieve distress for those in difficult circumstances. Theirs was a fine example to their family and friends.**

Before they died they established The Isabel and John Gilbertson Charitable Trust, with each of their children as trustees, to encourage their extended family to continue to care for and help others wherever possible.

Established in 2001, The Isabel and John Gilbertson Charitable Trust's commitment is to support the community through short-term emergency relief and long-term projects.

"We also have a strong interest in medical research," one of the trustees, Mr Peter Gilbertson said. "Our family has experienced first-hand the impact of illness. We understand that medical research can lead to new treatments for the prevention and treatment of diseases and can improve the health of millions of people."

Mr Gilbertson said each year the trustees of The Isabel and John Gilbertson Charitable Trust take considerable time to evaluate what they see as the priority needs and community projects that should be supported. "In this way, the trust ensures that the current and future generations of the Gilbertson family will be actively involved in supporting people and projects in the community," he said.

The Isabel and John Gilbertson Charitable Trust has supported the institute's research program since 2007.

Isabel and John Gilbertson in 2001, the year they established The Isabel and John Gilbertson Charitable Trust.

## The institute acknowledges the support of the following organisations

Australian Government

Victoria The Place To Be

The Atlantic Philanthropies

Australian Cancer Research Foundation

Bill & Melinda Gates foundation

Cancer Council Victoria

HFSP

HHMI

The Ian Potter Foundation

JDRF

Leukaemia Foundation

The Leukaemia & Lymphoma Society

National Breast Cancer Foundation

National Institutes of Health

Ramaciotti Supporting Biomedical Research

Victorian Breast Cancer Research Consortium Inc

Victorian Cancer Agency Linking research and patient care

wellcome trust

World Health Organization

## Mrs Margaret Johnson, supporting malaria research

**In January 1963 Mrs Margaret Johnson, then a 23-year-old high school teacher, travelled to Vanuatu to work on a church project to build a dormitory for a high school.**

"I was there for a month, and had taken chloroquine as prescribed by my GP, and returned to teaching in Australia. But three months later came the headaches and fever," Mrs Johnson said.

Initial blood tests found no evidence of malaria. It was her parents' doctor, a returned soldier from World War II who had seen malaria during service, who successfully diagnosed Margaret's illness.

Two to three years later, Mrs Johnson was reading a UNESCO magazine and learned how widespread malaria was in developing countries and how it affects people's lives.

"I realised that people with malaria do not have the energy to sow their crops for the next season and that people die of malaria. That shaped my thinking of donating to malaria research to support developing countries. You can relieve poverty if people can feed themselves."

Mrs Johnson's interest in the challenges facing developing countries spans nearly 50 years and she has donated to the institute's malaria research for more than 25 years.

"Although I experienced malaria first-hand, I have been well ever since," she said. "I have benefited from living in an affluent society and I feel strongly about supporting malaria research to benefit people in developing countries."

Mrs Margaret Johnson supports malaria research for the benefits it can bring to people in developing countries.

## Robert Evans, supporting governance and research

**The institute is fortunate to enjoy the support of community members who volunteer their knowledge, experience and time to advance research and discovery, volunteers such as Mr Robert Evans.**

For more than 20 years, Mr Evans was a member of the institute's investment committee, which protects and grows the institute's endowment to sustain research and discovery into the future. Mr Evans, who is now retired, worked in investment and stock broking and volunteered his expertise in financial management to the institute.

Mr Evans said he returned to Australia in 1987, after a number of years working overseas, looking to help not-for-profit organisations that made tangible contributions to improve people's lives. It was Mr Bruce Teele, then treasurer of the institute and chairman of the investment committee, who invited Mr Evans to join the committee.

"Bruce talked with me about the institute's research and its scientists and the discoveries that they were making," he said. "Becoming a committee member to do what I could to ensure this research continued wasn't a difficult decision to make."

It was while Mr Evans was on the committee that he decided to donate to the institute's research initiatives.

"In the finance area, clearly you work with money. People in the finance industry can earn a reasonably high income. I felt humbled that the scientists' salaries were not as large as mine and they were doing a lot more for humanity."

Mr Evans retired from the investment committee in 2007. He said he would have liked to stay on but, as he was taking a step back from the finance industry, he thought the time was right to let others closer to the industry take the lead.

"I became a donor because I could see and hear about the scientists doing staggering things for medical research. It made a big impact on me, and I continue to be a donor today," he said.

Mr Robert Evans, pictured right, and his wife Meredith with company secretary Mr Murray Jeffs. Mr Evans has contributed to the institute for more than 20 years.

## Donations $1000 and over

Estate of Eleanor Margrethe Albiston (The Stang Bequest)
Anonymous - NSW
Anonymous - Tas
Anonymous - Vic
Anonymous - Vic
Anonymous - Vic
Anonymous - Vic
Anonymous - Vic
Hazel & Pip Appel Fund
Estate of Lindsay James Baldy
Ms Shirley Bartlett
Ms Katherine I Behrend
Bell Charitable Fund
Berwick Opportunity Shop
BHP Billiton Matched Giving Program
Mr Angelo Bladeni
Estate of C H Boden
Estate of John Frederick Bransden
Harold and Cora Brennen Charitable Fund
Estate of Thomas, Annie, and Doris Burgess
Cardinia Beaconhills Golf Links
L R Cazaly Trust
Estate of George Collie
Commercial Albury Ladies Golf
Coolah Lady Golfers
Craven Investment Pty Ltd
Estate of the late Jean Ellen Craven
Mr Gordon Darling AC CMG
Mr Patrick Devlin
Mr Ronald F Diamond
Estate of Mavis Rae King Dick
Drakensberg Trust
Estate of Ethel Mary Drummond
Dr Janice Dudley
Thomas William Francis & Violet Coles Trust
Mr James R Gill
Ms Cecily Gilson
Estate of Keith Goldsbury
Estate of Winifred Florence Grassick
Mrs Jean T Hadges
Mr Robert Hain
Estate of Maxwell Gardiner Helpman
Estate of Sheila Mary Helpman
Mrs Jane Hemstritch
Mr Graham B Jackson
Ms Caroline Johnston
Mrs Chlorine Kluck
Estate of Laura Sampson Lamb
Estate of Margaret Liggins
Mr John B Little
Dr Darren Lockie
Dr Neville J McCarthy AO
Mrs Christine McConnell
Irene & Ronald MacDonald Foundation
Alan Gordon McMillen Arts Trust Gift Fund
Mrs Nina M Mace
Albert H Maggs Charitable Trust
Mr Damien Miller
Miriam Vale Golf Club Lady Members
Bettye Victoria Mitchell Fund
Estate of Florence Helen Winiberg Moden
Dame Elisabeth Murdoch AC DBE
Mrs Anne E Naylor
Ocean Shores Golf Club
Miss Lois E Oliver
Estate of Eva Orloff
Pambula-Merimbula Golf Club
Mrs Paddy Pearl
GT & L Potter Charitable Trust
Agnes Maude Reilly Charitable Trust
Estate of Margaret Lewis Reilly
Mr Dieter O Rinke
Ms Judy Rix
Mr Michael B Robinson AO
RobMeree Foundation
Mrs Margaret S Ross AM
Rotary Club of Eltham
Mrs Pam Sargood
Estate of the late Mary Annie Shearer
Jean Skea Memorial Trust
Nell & Hermon Slade Trust
Ms Pauline Speedy
State Trustees Limited
Ms Jenny Tatchell
Mr Kim Teoh
The William Angliss (Victoria) Charitable Fund
The Jack Brockhoff Foundation Ltd
The Decor Corporation Pty Ltd
The Dyson Bequest
The Isabel & John Gilbertson Charitable Trust
The Goldschlager Family Charitable Foundation
The Walter and Eliza Hall Trust
The J.H.A. Munro Foundation Ltd
The Nossal Family Trust
The Lady Tata Memorial Trust
The Victoria Golf Club Ltd
Mr Christopher Thomas
Thomas Family Fund
Mrs Olive Thurlby
Estate of Lila Joyce Underwood
Vincentia Golf Club Lady Members
Joe White Bequest
Ms Marjorie E Wilks
Estate of Lorraine Florence Williams
Mr David A Williamson
Estate of Emily Vera Winder
Estate of Rosemary Anne Woodfull
Yarra Yarra Golf Club
Estate of Florence Mary Young

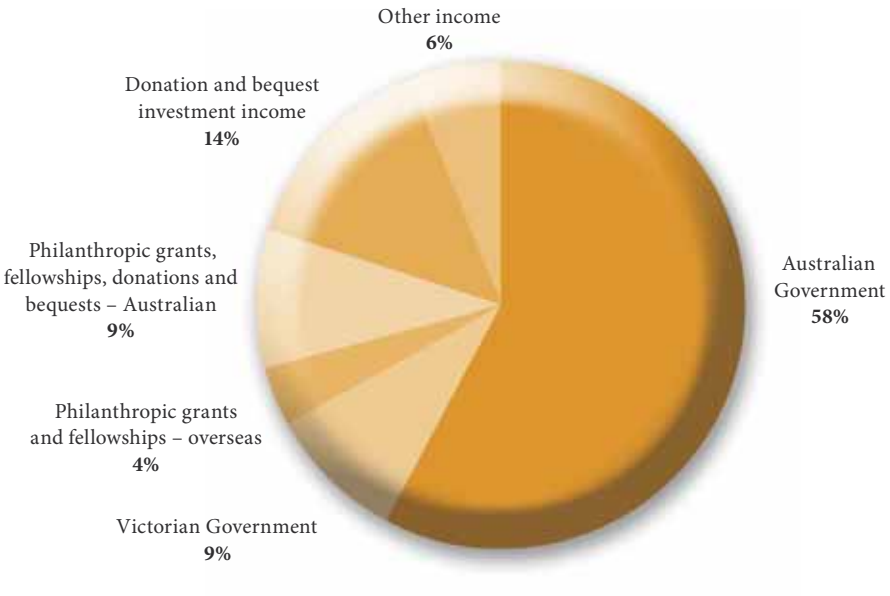
## New donations of capital received in the 2010–11 financial year

Anonymous – Seminar Award
Tim Bates Memorial Diabetes Research Fund
Joy & Desmond Cory Cancer Research Fund
DA Craven Memorial Fund
Estates of the late JE Craven & late MA Shearer
Estate of the late MRK (Rae) Dick
Estate of the late Nina May Mace
Estate of the late Bettye Victoria Mitchell
Estate of the late RHW Moden
Sir Gustav Nossal Fund
Barbara Parker Memorial Fund
Paddy Pearl Fund
Lyndal & Jean Skea Leukaemia Fund
Estate of the late RM Tink

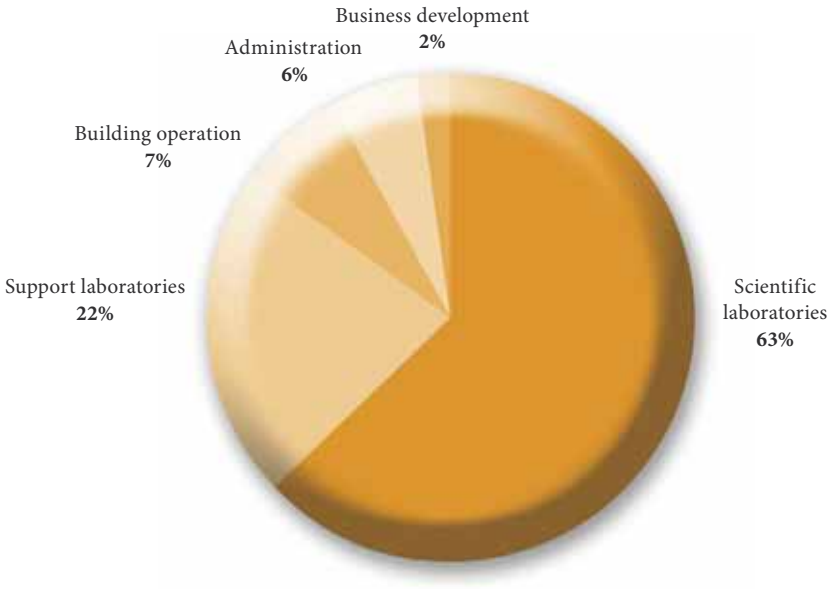
The full list of the institute's permanent named capital funds is on the accompanying CD.

# The year at a glance

## Income*




## Expenditure




## The year in brief

| | 2011 | 2010 |
|---|---|---|
| Income for research ($000) (excluding investment income)* | **70,748** | **64,233** |
| Donation and bequest investment income ($000) | **11,486** | **9,278** |
| Expenditure on research ($000) | **79,124** | **74,182** |
| Net surplus (deficit) from research ($000) | **3,110** | **(671)** |
| Number of staff and visiting scientists | **585** | **558** |
| Number of postgraduate students | **135** | **103** |
| Total staff and students (EFTs) | **720** | **661** |

*Excluding income for institute redevelopment project of $136,000 (2010: $2,063,000)

## Statistical summary for the year ended 30 June

| | 2011 $,000s | 2010 $,000s | 2009 $,000s | 2008 $,000s | 2007 $,000s |
|---|---|---|---|---|---|
| **Research revenue** | | | | | |
| Australian Government | 45,973 | 39,291 | 37,409 | 33,446 | 29,230 |
| Victorian Government | 6,842 | 7,638 | 7,355 | 8,229 | 9,205 |
| Foreign governments | 557 | 953 | 543 | 443 | 776 |
| **Government revenue** | **53,372** | **47,882** | **45,307** | **42,118** | **39,211** |
| Industrial grants and contracts | 1,846 | 3,518 | 3,722 | 3,847 | 2,580 |
| Philanthropic grants and fellowships - Australia | 3,830 | 3,644 | 3,440 | 2,370 | 2,049 |
| Philanthropic grants and fellowships - international | 3,235 | 4,399 | 6,551 | 6,208 | 6,193 |
| Investment income [1,2] | 11,486 | 9,278 | 10,007 | 8,561 | 7,543 |
| Royalty income | 2,513 | 1,071 | 1,356 | 1,943 | 3,198 |
| General revenue | 2,647 | 2,761 | 3,140 | 2,238 | 2,425 |
| Donations and bequests | 3,305 | 958 | 1,178 | 977 | 1,254 |
| **Non-government revenue** | **28,862** | **25,629** | **29,394** | **26,144** | **25,242** |
| **Total revenue for research** | **82,234** | **73,511** | **74,701** | **68,262** | **64,453** |
| **Research expenditure and financial results** | | | | | |
| Staff costs | 54,799 | 48,938 | 45,419 | 42,903 | 39,099 |
| Laboratory operating costs | 15,424 | 16,310 | 15,817 | 15,068 | 12,934 |
| Laboratory equipment | 2,862 | 2,474 | 2,591 | 2,271 | 2,192 |
| Building operations | 4,353 | 4,356 | 4,551 | 4,152 | 4,171 |
| Administration | 1,002 | 1,225 | 1,485 | 1,375 | 1,406 |
| Business development | 684 | 879 | 1,410 | 1,109 | 1,325 |
| **Total research expenditure** | **79,124** | **74,182** | **71,273** | **66,878** | **61,127** |
| **Results from research activities** | **3,110** | **(671)** | **3,428** | **1,384** | **3,326** |
| **Other income** | | | | | |
| Profit on sale of long-term investments [3] | 7,712 | 1,151 | 1,372 | 5,260 | 9,072 |
| Donations and bequests | 1,566 | 2,120 | 9,879 | 34,738 | 1,524 |
| Grants and donations for capital works [1] | 117 | 428 | 492 | 2,547 | 1,340 |
| **Total other income** | **9,395** | **3,699** | **11,743** | **42,545** | **11,936** |
| **Other expenses** | | | | | |
| Loss on impairment write down of long-term investments | (2,945) | (203) | (8,417) | (9,336) | – |
| Depreciation and amortisation | (6,375) | (3,877) | (3,025) | (2,834) | (3,270) |
| **Total other expenses** | **(9,320)** | **(4,080)** | **(11,442)** | **(12,170)** | **(3,270)** |
| **Net operating surplus** | **3,185** | **(1,052)** | **3,729** | **31,759** | **11,992** |
| **Capital funds** | | | | | |
| Permanent invested capital funds | 134,457 | 129,802 | 126,475 | 115,072 | 75,561 |
| General funds | 138,752 | 90,534 | 35,998 | 25,814 | 31,404 |
| Royalty fund | 16,788 | 14,823 | 14,294 | 14,142 | 13,243 |
| Leadership fund | 16,182 | 15,873 | 15,672 | 15,226 | 13,881 |
| Asset revaluation reserve | 38,812 | 37,961 | 25,952 | 42,297 | 58,003 |
| **Total funds** | **344,991** | **288,993** | **218,391** | **212,551** | **192,092** |
| **Capital expenditure** | | | | | |
| **Property, plant and equipment** | **53,579** | **64,516** | **17,286** | **10,712** | **3,396** |
| **Staff numbers: (equivalent full-time) at 30 June** | **2011** | **2010** | **2009** | **2008** | **2007** |
| **Scientific research staff:** | | | | | |
| – Senior faculty | 64 | 52 | 52 | 50 | 54 |
| – Other | 147 | 143 | 156 | 130 | 112 |
| – Visiting scientists | 16 | 14 | 28 | 24 | 22 |
| **Supporting staff:** | | | | | |
| – Laboratories and all services | 358 | 349 | 323 | 315 | 326 |
| **Total staff and visiting scientists** | **585** | **558** | **559** | **519** | **514** |
| **Students** | **135** | **103** | **68** | **67** | **73** |
| **Papers published** | **250** | **249** | **246** | **224** | **241** |

1. Excluding funds for WEHI redevelopment project

2. Income excludes share buy back dividends in 2011 ($4.75M) and 2007 ($7.93M)

3. Income includes share buy back dividends in 2011 ($4.75M) and 2007 ($7.93M)

## A story of two generations

**Mrs Elizabeth Jenkins was in her early teens when her mother, Mrs Pamela Holliday, placed a copy of the Walter and Eliza Hall Institute annual report on the family table and said to her, "Here, have a look".**

"That's how it began," said Mrs Jenkins. "Each year after that the Walter and Eliza Hall Institute annual report was left on the table for me to peruse."

A pre-school teacher, Mrs Holliday started teaching in Melbourne at the end of World War II. Mrs Holliday taught generations of children over the next 40 years, at times teaching two generations in the one family.

"Early in mum's career, some of the children came from families that were really struggling and mum was involved in washing and providing clothes for these children," Mrs Jenkins said. "At mum's funeral, a lot of fellow teachers and supervisors said how inspirational she was, and how much she gave back to life."

A donor to the Walter and Eliza Hall Institute for more than 30 years, Mrs Holliday also made a gift in her will to the institute. "Mum made a bequest to support the institute's medical research because she wanted to help people who were suffering," Mrs Jenkins said. "She really believed in giving back to the community."

Mrs Holliday died in 2007, aged 82. Now, her daughter Elizabeth finds her life mirroring some of her mother's interests. With a science degree from The University of Melbourne, Mrs Jenkins' career has included supervising teams in data centres for two global corporations. "Then, three years ago, I thought about what I wanted to do next," she said. "I decided I wanted to be a primary school teacher, which I now am, and I love it."

Like her mother, Mrs Jenkins became a bequestor to the institute. "I think it's important to support organisations that are doing amazing research to benefit our health," she said. "I like the transparency of the institute, the way it is opening its doors to the community and saying, 'If you're interested, come in and have a look, which I did recently on a discovery tour'."

Mrs Jenkins attended an update meeting and lunch for bequestors, hosted by institute director Professor Doug Hilton. Her guest was her daughter, Emily, a medical student. Emily has spent her gap year travelling to developing countries, including in Africa, and observed the impact of malaria in the community, a disease that is one of the institute's research priorities.

Mrs Elizabeth Jenkins (left) and her mother, the late Mrs Pamela Holliday (right), have both left bequests to the institute.

## A gift in your will to medical research

Medical research is vital to improving healthcare and quality of life.

Researchers at the Walter and Eliza Hall Institute of Medical Research have made several discoveries that have improved health outcomes for millions of people.

A gift in your will to the Walter and Eliza Hall Institute is a lasting gift that will support our research efforts to improve human health with better prevention, detection and treatment of disease.

For a confidential discussion, please contact
Deborah Cutts, Head of Fundraising,
email cutts@wehi.edu.au or phone (03) 9345 2912.

FIAT LUX
Walter+Eliza Hall
Institute of Medical Research

**Walter and Eliza Hall Institute of Medical Research**
1G Royal Parade Parkville VIC 3052
Tel: (03) 9345 2555 Fax: (03) 9347 0852
**www.wehi.edu.au**

# CD-ROM

**The Walter and Eliza Hall Institute Annual Report 2010-11 CD-ROM contains a searchable PDF of the full annual report as well as the following:**

## Discovery

Staff photographs for each of the research divisions and the lists of national and international exchanges undertaken by staff within those divisions

Full publications list

## Education

Full list of PhD and Honours projects in progress

List of vacation scholars, UROP students and overseas research trainees

List of presentations that were given as part of our Wednesday seminar program and Postgraduate Lecture Series

## Engagement

Staff service to the scientific and wider community

WEHI.TV animations *Breast Stem Cells*, *Control of Breast Stem Cells* and *Origin of Breast Cancer*

## Sustainability

Full financial statements

Membership lists of institute and board committees

Full staff list

Printed in Australia with soy based inks on 100% recycled fibre, FSC certified, carbon neutral paper.