Walter+Eliza Hall
Institute of Medical Research

DISCOVERIES FOR HUMANITY

ANNUAL REPORT 2016

CANCER

IMMUNE DISORDERS

INFECTIOUS DISEASE

CONTENTS

We acknowledge the traditional owners and custodians of the land on which our campuses are located, the Wurundjeri people of the Kulin nation, and pay our respects to their elders past and present.

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Produced by the Walter and Eliza Hall Institute's Communications and Marketing department

OUR MISSION

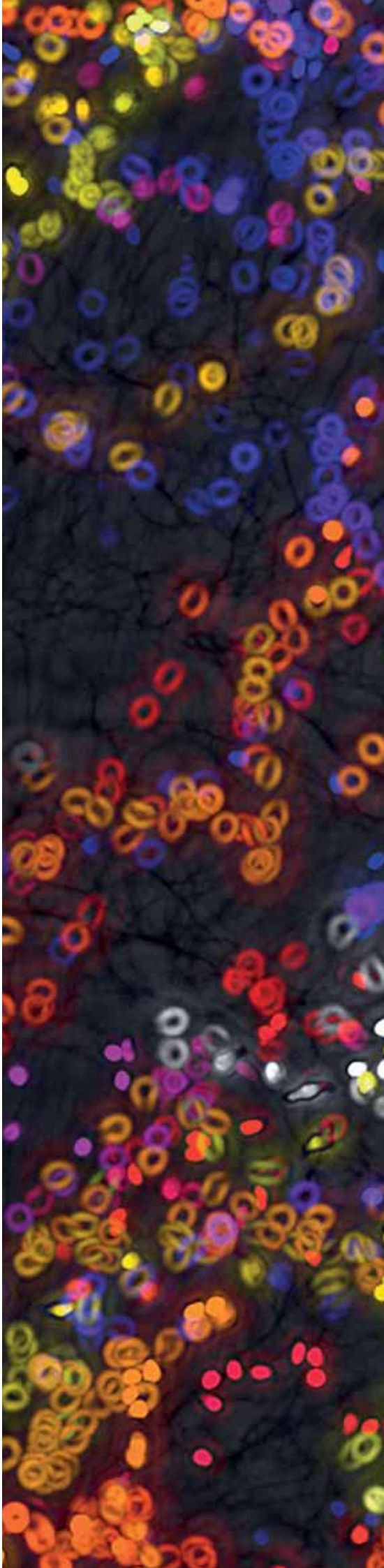
Mastery of disease through discovery

OUR VISION

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

OUR VALUES

- **Pursuit of excellence**
- **Integrity and mutual respect**
- **Collaboration and teamwork**
- **Creativity**
- **Accountability**
- **Contribution to society**



PRESIDENT'S REPORT

The Institute has entered its second century with gusto.

As reflected in our *Strategic Plan 2015-2020*, we have clarity of purpose and are confident we have the scientific leadership and excellence, supported by the necessary technology and financial resources, to continue to make significant discoveries in the future.

There have been many exciting advances in the past year. One of the most notable was the approval of anti-cancer drug venetoclax for use in treating people with certain forms of leukaemia. Investment in new technology platforms, notably structural biology and medicinal chemistry, was critical in this 30-year odyssey. So was the collaboration between more than 100 Institute scientists, and others based elsewhere, and biotechnology companies AbbVie and Genentech, a member of the Roche Group.

One of the board's immediate challenges is to ensure that any financial returns from this breakthrough are invested in ways that ensure the Institute delivers on its plans and continues making discoveries for humanity.

The Institute was founded on extraordinary philanthropy and much of what we achieve continues to be based on the generosity of many. Whether through trusts and foundations, disease focused fundraisers or gifts from individuals, we would not otherwise be what we are today. While government funding is significant, it is philanthropic support that makes the difference for our researchers. Our Centenary campaign continues and we now have 19 Centenary Fellowships that are enabling the next generation of scientists to pursue vital research questions.

"THE INSTITUTE WAS FOUNDED ON EXTRAORDINARY PHILANTHROPY AND MUCH OF WHAT WE ACHIEVE CONTINUES TO BE BASED ON THE GENEROSITY OF MANY"

Finally, my thanks to all board members for their contributions. Despite several planned changes in the past year we continue to have a highly engaged group. Members contribute their experience gained in diverse but relevant backgrounds and the discussions are always lively and conducted with open minds.

To those who departed, my special thanks for their extraordinary commitment and contributions. In Steven Skala (vice president for 12 years), Mike Fitzpatrick, Catherine Walter and Dr Gareth Goodier, we have lost 51 years combined experience. However, I am confident that our new board members, John Dyson, Marie McDonald and Carolyn Viney, will be outstanding successors, as will Jane Hemstritch as our new vice president.

Mr Christopher Thomas AM
President
Walter and Eliza Hall Institute
of Medical Research

DIRECTOR'S REPORT

2016 was an exciting year at the Institute. There were many advances in our research programs, in our collaborations and in existing and new education partnerships.

One of the highlights was to see a new medicine, venetoclax, approved as a treatment for people with certain forms of leukaemia. The fundamental research into the regulation of cell survival and cell death underpinning this development commenced at the Institute in the 1980s. The translational journey highlights the power of long-term, multidisciplinary research, and the importance of strong international and local collaborations. I am confident that the lessons we have learned and the inspiration we have gained from this journey will ensure other basic scientific discoveries are rapidly translated to clinical benefit.

Institute research teams also made important discoveries that have shed light on fundamental biological processes and which have moved us closer to better treatments for other diseases. These breakthroughs include revealing a potential new approach to prevent breast cancer in women who carry the *BRCA1* risk gene; using the genome sequence of the scabies and malaria parasites to identify potential new approaches to combat these globally significant diseases; and structural biology studies of a form of insulin found in the venom of cone snails, that may lead to more efficient therapies for diabetes.

"OUR STRONG COLLABORATIVE CULTURE CONTINUES TO THRIVE"

Our strong collaborative culture continues to thrive. Within the Institute, bioinformatics, computational biology, structural biology and medicinal chemistry, when combined with our traditional strengths in molecular biology, cell biology and physiology, are enabling a more detailed and meaningful understanding of medical biology than ever before.

At the local level, the relocation of the Peter MacCallum Cancer Centre to Parkville has allowed us to strengthen our collaborations through the Victorian Comprehensive Cancer Centre.

A landmark in the Institute's international collaborations was the signing of a memorandum of understanding for the establishment of a new translational research centre in Nanjing, China, which will enhance our preclinical and clinical research capabilities.

Great research requires great people, and we are committed to ensure an exceptional working environment for all. Central to this are initiatives to enhance diversity and gender equity, which we continue to champion within the Australian research sector.

It was with deep sadness in November that we farewelled Dr Margaret Holmes, a pioneer for Australian women in medical sciences and the devoted first general manager of the Institute. Margaret's affiliation with the Institute spanned almost 80 years, and she was a friend to many. Vale and thank you Margaret. Thank you also to our board and all of our staff and students, who, whether they have been with us for a few weeks or many decades, make the Institute such a vibrant place to work.

Professor Douglas Hilton AO
Director
Walter and Eliza Hall Institute
of Medical Research

Board president Mr Christopher Thomas (left) and Institute director Professor Douglas Hilton

INSTITUTE HIGHLIGHTS

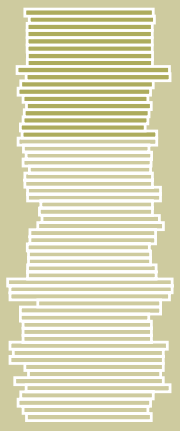
1077
staff and students

50+
diseases impacted by Institute research

100
national and international trials based on Institute discoveries

92
publications with impact factor >10

429
publications



>300
projects

>100
clinical trials

22
Clinician-scientists

27
PhD students with medical training

>4800
event attendees

>30
million patients benefited worldwide

44
patents granted in 2016

WEHI movies

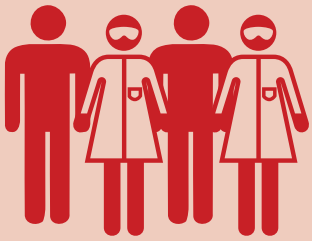
>325,000
views of WEHIMovies YouTube channel

$18.736M
raised in philanthropic gifts

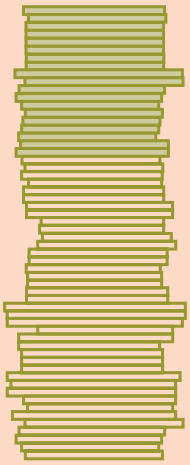
Material transfer agreements with collaborators in **96** countries

94c per $1
of philanthropic funding directly supports research

28
consumer buddies paired with research groups



225
students

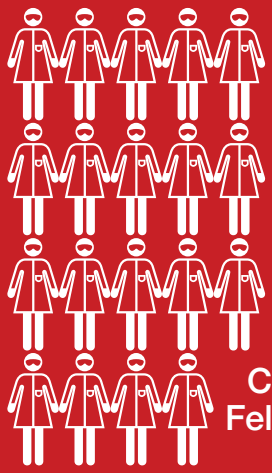


25
publications with student authors with impact factor >10

89
publications with student authors

3 organisations working to improve Indigenous health and education outcomes supported

4 events to celebrate Aboriginal and Torres Strait Islander history and culture



19
Centenary Fellowships pledged at 31 December 2016

Sources of income **2016**

45% Australian Government

7% Victorian Government

21% Philanthropic grants, donations and bequests

12% Investment income

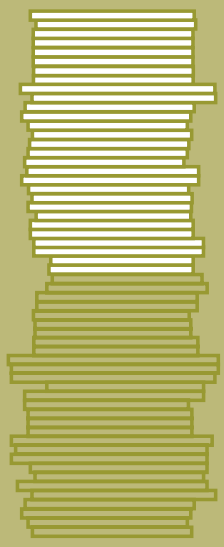
15% Other income

4 reconciliation-focused seminars and events

5 Aboriginal and Torres Strait Islander interns

55 Aboriginal and Torres Strait Islander school students visited the Institute

>50%
of publications related to clinical translation



HEALTH IMPACTS

The Institute is committed to making fundamental scientific discoveries that can be translated to better treatments, bringing real benefits to the community on a global scale. Clinical trials based on discoveries made at the Institute include trials of vaccines for coeliac disease, diabetes and malaria; trials of new anti-inflammatory agents; and trials of a new class of anti-cancer drugs, called BH3-mimetics, for treating people with leukaemia and other cancers.

- **Cancer**
  - Bowel cancer
  - Brain cancer
  - Breast cancer
  - Leukaemia
  - Lung cancer
  - Lymphoma
  - Melanoma
  - Myeloma
  - Myeloproliferative disease
  - Ovarian cancer
  - Pancreatic cancer
  - Prostate cancer
  - Rare cancers
  - Stomach cancer
- **Immune disorders**
  - Allergy
  - Asthma
  - Autoinflammatory diseases
  - Coeliac disease
  - Inflammatory bowel disease
  - Lupus
  - Multiple sclerosis
  - Primary immune deficiencies
  - Psoriasis
  - Rheumatic fever and rheumatic heart disease
  - Rheumatoid arthritis
  - Sepsis
  - Type 1 and type 2 diabetes
- **Infectious disease**
  - Filariasis
  - Giardiasis
  - Hepatitis B
  - HIV
  - Influenza
  - Leishmaniasis
  - Malaria
  - Scabies
  - Toxoplasmosis
  - Tuberculosis

ABOUT THE INSTITUTE

The Walter and Eliza Hall Institute is Australia's oldest medical research institute. It was founded in 1915 with financial support from a trust established by Eliza Hall, following the death of her husband Walter. The vision was for an institute that 'will be the birthplace of discoveries rendering signal service to mankind in the prevention and removal of disease and the mitigation of suffering'.

Throughout the Institute's history its researchers have focused on understanding the fundamental principles of medical biology and using this knowledge to mitigate disease.

Our current researchers and students continue to work on solving basic science questions through curiosity-driven research. We are committed to innovative science that expands and improves our understanding of basic human biology and the disruptions to systems that cause disease. Our scientists also undertake blue-sky research that creates and explores new areas of biology.

Three nationally and globally significant areas of health have been long-term, central interests of our research:

- cancer – understanding the basic processes that are disrupted to generate cancer cells and how these can be targeted to treat disease;
- immune disorders – discovering how the body fights infection, and how errors in the immune system lead to disease; and
- infectious diseases – with a focus on globally significant pathogens, especially malaria and chronic infections.

We take a multidisciplinary approach to addressing major research questions, integrating expertise in bioinformatics, clinical translation, computational biology, epidemiology, genomics, medicinal chemistry, personalised medicine, proteomics, structural biology and systems biology.

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

DOING GREAT SCIENCE

Our success rests on our capacity to advance scientific knowledge and health outcomes through basic research and translation.

Our strategy builds on our existing strengths and emerging opportunities.

PhD student Ms Rebecca Delconte's research aims to enhance how our immune system can fight cancer, an approach called cancer immunotherapy.

CANCER AND HAEMATOLOGY

The Cancer and Haematology division is working to understand the production and function of the billions of blood cells used each day to fight infections and repair tissues, and how they are regulated at the molecular level.

Our aim is to understand how these processes are disrupted in disease, to aid in developing new therapies for immune and inflammatory diseases, blood clotting disorders and cancers.

Deciphering childhood leukaemia

Research advances have greatly improved the outcomes for children with leukaemia in the past two decades. Unfortunately some children respond poorly to current treatments.

Thanks to support from the Victorian Cancer Agency and The Alfred Felton Bequest, Dr Ian Majewski is using genomics to predict better treatment approaches for children with leukaemia.

With collaborators at the Murdoch Children's Research Institute, Dr Majewski's team used new sequencing technologies to uncover previously unrecognised gene changes in childhood leukaemia. This information will be used to improve the design of clinical trials and develop new personalised therapies for children with currently untreatable forms of leukaemia.

Improving myeloma treatments

Institute researchers discovered a new target for treating multiple myeloma, an incurable bone marrow cancer diagnosed in more than 1700 Australians each year.

Dr Jianan Gong, Dr David Segal, Ms Yuan Yao, Professor Andrew Roberts and Professor David Huang, working with researchers at the Australian Centre for Blood Diseases, Monash University and the Alfred Hospital, revealed that the majority of myelomas rely on a protein called MCL-1 to survive.

The team also showed that switching off MCL-1 has the potential to be an effective new treatment approach for the majority of patients with myeloma. The Institute is currently collaborating with international industry partners on new approaches to target MCL-1 for treating disease.

Gift of hope for childhood leukaemia

A gift from the Jakob Frenkiel Charitable Trust is supporting research to improve the treatment of childhood acute lymphoblastic leukaemia (ALL), the most common cancer in Australian children.

While treatments for ALL have improved in recent years, some children respond poorly to, or relapse following, first-line treatment. Clinician-scientist Dr Seong Lin Khaw is investigating whether childhood ALL could be treated with promising new anti-cancer agents called BH3-mimetics, which target the proteins that keep ALL cancer cells alive.

In collaboration with scientists at the Children's Cancer Institute, Dr Khaw's research is pinpointing the subtypes of ALL that will best respond to BH3-mimetics, and which of these anti-cancer agents may offer the optimal treatment for these diseases.

Health impact

Cancers: leukaemia, lymphoma, myeloma, myeloproliferative diseases

Immune disorders: asthma, Crohn's disease, rheumatoid arthritis

Other areas: blood clotting diseases, heart disease and stroke, personalised medicine

Division heads

Professor Warren Alexander

Professor Nick Nicola

Laboratory heads

Dr Jeff Babon

Dr Stefan Glaser

Professor David Huang

Dr Emma Josefsson

Dr Matthew McCormack

Dr Ian Majewski

Professor Andrew Roberts

Dr Samir Taoudi

Professor Christine Wells

52 publications

39 staff

10 students

10 clinicians

Australian approval for new anti-leukaemia treatment

A hallmark of cancer cells is their ability to evade the normal process of cell death. Almost 30 years ago Institute researchers discovered that a protein called BCL-2 confers longevity on many types of cancer cells, pinpointing it as an ideal target for anti-cancer therapies.

Professor Andrew Roberts and Dr Mary Ann Anderson, clinician-scientists at the Institute and clinical haematologists at The Royal Melbourne Hospital, have been part of the clinical research team leading studies of a new anti-cancer agent, venetoclax. This drug, co-developed for clinical use by US pharmaceutical companies AbbVie and Genentech, a member of the Roche group, was discovered by AbbVie scientists as part of a joint research collaboration with Walter and Eliza Hall Institute scientists.

"IN THE FUTURE THIS MAY HELP TO PERSONALISE TREATMENT FOR CLL TO MATCH THE RIGHT TREATMENT TO A PATIENT'S DISEASE"

In a world-first clinical trial conducted at sites including The Royal Melbourne Hospital and Peter MacCallum Cancer Centre, venetoclax was studied in people with advanced forms of chronic lymphocytic leukaemia (CLL) when conventional treatment options had been exhausted, Professor Roberts said.

Dr Anderson, Professor David Huang, Professor Roberts and colleagues in Cancer and Haematology division have investigated whether CLL patients' response to venetoclax can be predicted by laboratory tests. Dr Anderson said the research, which was performed in collaboration with Dr Ian Majewski and clinical colleagues, aimed to define pathology tests that can be used to rapidly identify those people who may stand to benefit from venetoclax.

"We are seeking to work out why some CLL patients do not respond as well as others to venetoclax," she said. "In the future this may help to personalise treatment for CLL to match the right treatment to a patient's disease."

Venetoclax has now been approved for use in the US, the European Union and Australia treating certain, high-risk forms of CLL, and is in clinical trials for other forms of blood and breast cancer.

Collaborating divisions

Cancer and Haematology, ACRF Chemical Biology, Molecular Genetics of Cancer

Collaborating organisations

AbbVie, Dana-Farber Cancer Institute (US), Genentech (a member of the Roche Group), Memorial Sloan Kettering Cancer Center (US), Peter MacCallum Cancer Centre, The Royal Melbourne Hospital, Swedish Medical Center, Seattle (US), University of Arizona (US), University of California, San Diego (US), University of Texas M.D. Anderson Cancer Center (US), Washington University, St. Louis (US), Weill Cornell Medical College (US)

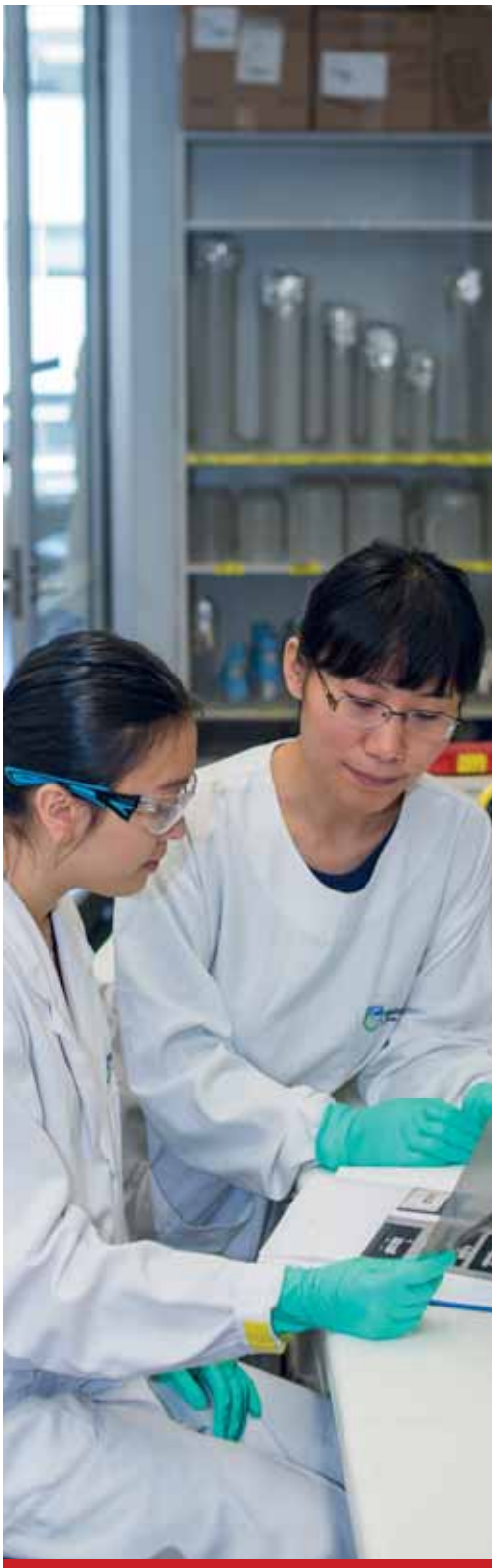
Funding partners

American Society of Clinical Oncology, Australian Cancer Research Foundation, Australian National Health and Medical Research Council, Cancer Council Victoria, Leukemia & Lymphoma Society (US), National Institutes of Health (US), Victorian Cancer Agency, Victorian Government Operational Infrastructure Support Program, Webster Bequest

More information

Roberts AW *et al*. Targeting BCL2 with Venetoclax in Relapsed Chronic Lymphocytic Leukemia. *New England Journal of Medicine*. 2016 Jan 28;374(4):311-22

Anderson MA *et al*. The BCL2 selective inhibitor venetoclax induces rapid onset apoptosis of CLL cells in patients via a TP53-independent mechanism. *Blood*. 2016 Jun 23;127(25):3215-24



Dr Jianan Gong (right) was part of a team that discovered that the majority of myelomas rely on a protein called MCL-1 to survive. Their research suggests that MCL-1 may be a valuable therapeutic target for myeloma, which is an incurable blood cancer. Dr Gong is pictured with undergraduate student Ms Winnie Zhang.

Centenary Fellowship to unravel how platelets promote cancer

Tiny blood cells called platelets quickly form a plug to seal wounds when we suffer a cut or other injury, protecting us from bleeding to death.

For the past 15 years Dr Emma Josefsson's research has focused on the biology of platelets: how they are produced, how their numbers in the blood are regulated, and how they function in health and disease.

Recently, Dr Josefsson has begun to investigate how platelets influence cancer formation and spread.

"THIS COULD ALLOW A NEW APPROACH TO TREATING CANCER"

Dr Josefsson said that since the 1960s low platelet numbers in laboratory models and platelet-inhibiting therapies, such as aspirin, had been linked to a reduced risk of tumour spread (metastasis).

"Although low platelet numbers may be linked to a lower risk of metastasis, low platelet counts and platelet-inhibiting therapies are also associated with increased risk of bleeding," she said.

"A better understanding of the interactions between platelets and tumour cells is needed. Our hope is that this would reveal how we could develop targeted therapies that stop cancers from spreading while maintaining normal blood clotting. This could allow a new approach to treating cancer."

The Lorenzo and Pamela Galli Centenary Fellowship in cancer research has provided a boost to Dr Josefsson's research into the role of platelets in cancer. This five-year fellowship was donated by the Lorenzo and Pamela Galli Charitable Trust in honour of Mr Lorenzo Galli, a Victorian businessman and vigneron who died of cancer.

Dr Josefsson said the funding security provided by this Centenary Fellowship meant that she could focus fully on an ambitious, long-term program of research.

"The concept of platelets contributing to cancer growth and spread is poorly understood," she said. "The fellowship means that over the next five years I can pursue answers to a number of important questions that will advance this field, hopefully bringing it closer to clinical applications, and improving cancer therapies."

Platelets are tiny cells that are essential for blood clotting. The five-year Lorenzo and Pamela Galli Centenary Fellowship in cancer research is enabling Dr Emma Josefsson to investigate whether platelets contribute to the spread of cancer. Dr Josefsson (left) is pictured explaining her research to a tour of World Cancer Congress delegates.

ACRF STEM CELLS AND CANCER

The ACRF Stem Cells and Cancer division is focused on breast, ovarian and lung cancers. Our aim is to understand normal organ development and perturbations that give rise to cancer in order to discover new therapies.

Secrets of lactation revealed

The production of milk within the mammalian breast evolved to enable the nurturing of newborns. During pregnancy the mammary gland undergoes substantial growth and changes that enable milk production.

Dr Anne Rios and Dr Nai Yang Fu have used advanced 3D imaging technology to gain new insights into the changes that occur within breast cells at the onset of lactation. They revealed that, during late pregnancy, the breast generates vast numbers of cells with two nuclei – structures within cells that contain the genetic material – and at the cessation of lactation these cells disappear. These 'bi-nucleated' cells were found in five diverse mammalian species and the team speculate that they are critical for maximising milk production.

New insights into lung cancer

A three-year PhD scholarship from Lung Foundation Australia is supporting Ms Casey Ah-Cann's research into how the lung develops, and how this process is corrupted in lung cancer.

Ms Ah-Cann, with supervisors Dr Marie-Liesse Asselin-Labat and Associate Professor Marnie Blewitt, is investigating proteins that alter gene expression within cells in the developing lung. In addition to revealing how this complex organ forms, she aims to determine whether lung cancer develops through a similar molecular process. Understanding the proteins that regulate gene expression in lung cancer may lead to new, targeted treatments that could improve the outcomes for people with this disease.

National award for breast cancer research

Professor Jane Visvader was awarded the 2016 Lemberg Medal, the highest honour of the Australian Society of Biochemistry and Molecular Biology (ASBMB).

Research led by Professor Visvader has resulted in several advances in the understanding of how the breast forms – including the isolation of the long-sought mammary stem cell – and the links between normal tissue development and breast cancer.

Professor Visvader, joint head of the ACRF Stem Cells and Cancer division, has co-led the Institute's breast cancer research program since its establishment in 1998. Her team has also revealed new approaches to the prevention and treatment of breast cancer.

Health impact

Cancers: breast cancer, lung cancer, ovarian cancer, rare cancers

Other areas: personalised medicine, chronic lung disease

Division heads

Professor Geoff Lindeman

Professor Jane Visvader

Laboratory heads

Dr Marie-Liesse Asselin-Labat

Associate Professor Clare Scott

Dr Kate Sutherland

25 publications

37 staff

11 students

8 clinicians

PhD student Ms Clare Weeden has discovered the stem cells that are thought to give rise to lung squamous cell carcinoma, a type of cancer with poor prognosis.

This finding may lead to better approaches for prevention, early detection and treatment of this cancer.

‘Cell of origin’ provides clues for early detection of lung cancer

Lung cancer causes more deaths than any other cancer in Australia.

Approximately 30 per cent of lung cancers are squamous cell carcinomas, a cancer that has a very poor prognosis, typically because it is discovered at a late stage when the cancer is inoperable and responds poorly to anti-cancer treatments.

Dr Marie-Liesse Asselin-Labat and Ms Clare Weeden discovered the cells that are thought to give rise to lung squamous cell carcinomas.

Using donated lung tissue obtained through the Victorian Cancer Biobank, Dr Asselin-Labat and Ms Weeden isolated lung stem cells. These stem cells are long-lived cells that give rise to other types of cells within the lung, enabling its repair and rejuvenation over a lifetime.

> “WE SAW A PATTERN THAT INDICATED LUNG STEM CELLS WERE CLOSELY RELATED TO CANCER CELLS”

In a study inspired by the Institute’s successful breast stem cell program, the researchers studied the function of these lung stem cells to understand how lung cancer forms.

Ms Weeden said the team were able to isolate stem cells, called basal stem cells, from the lung airways. “By looking at the genes these stem cells used we saw a pattern that indicated lung stem cells were closely related to cancer cells in lung squamous cell carcinomas,” she said.

Squamous cell carcinomas are a form of lung cancer that predominantly affects smokers and ex-smokers.

Dr Asselin-Labat said the team had unearthed some of the first evidence linking flawed DNA repair in lung basal stem cells with cancer development.

“We discovered that when exposed to harmful chemicals, such as those found in cigarette smoke, basal stem cells tried to repair any damage they suffered,” she said. “However, there was a problem: the rapid repair process they employ is riddled with errors.

“The poor quality of DNA repair in basal stem cells could contribute to an accumulation of genetic mutations that eventually leads to them becoming cancerous,” Dr Asselin-Labat said.

Ms Weeden said the team hoped to use their findings to develop better approaches to prevent or treat lung squamous cell carcinoma. “There is a great need for better treatments for lung cancer,” she said. “We hope that our work will be a gateway to new, more tailored therapies.”

Collaborating divisions

ACRF Stem Cells and Cancer, Bioinformatics

Collaborating organisations

Monash University, the University of Melbourne

Funding Partners

Australian National Health and Medical Research Council, Australian Postgraduate Award, Cancer Therapeutics CRC, The Royal Melbourne Hospital, The Harry Secomb Foundation, the Victorian Cancer Agency, Victorian Cancer Biobank, Victorian Government Operational Infrastructure Support Program and the Viertel Charitable Foundation

More information

Weeden CE *et al*. Lung basal stem cells rapidly repair DNA damage using the error-prone non-homologous end joining pathway. *PLoS Biol.* 2017 Jan 26;15(1):e2000731

Rare cancer research boosted by Centenary Fellowships

Cancers that affect fewer than six people per 100,000 in the population each year are considered 'rare'. Though rare individually, rare cancers collectively account for about one in five cancers diagnosed in Australia and almost one third of cancer deaths in Australia.

Institute clinician-scientist Associate Professor Clare Scott said rare cancers were often diagnosed at an advanced and more difficult to treat stage.

"Health professionals may not recognise the symptoms of a rare cancer, or may not be aware of the need for specific investigations," said Associate Professor Scott, who is also a medical oncologist at the Royal Melbourne Hospital and the Peter MacCallum Cancer Centre.

> "UNFORTUNATELY TREATMENTS FOR RARE CANCERS HAVE NOT ADVANCED AT THE SAME PACE AS TREATMENTS FOR MORE COMMON CANCERS"

"As there are only a few patients diagnosed with each type of rare cancer at each hospital or cancer research centre, many rare cancer types have not been well studied.

"Unfortunately treatments for rare cancers have not advanced at the same pace as treatments for more common cancers."

Associate Professor Scott is leading new research to develop novel strategies to select the best treatments for patients diagnosed with rare cancers.

Support from the Stafford Fox Medical Research Foundation has enabled establishment of the Stafford Fox Rare Cancer Research Program at the Institute, including the appointment of two Centenary Fellows.

The Stafford Fox Centenary Fellowship in rare cancer research was awarded to Dr Holly Barker, and the Stafford Fox Centenary Fellowship in bioinformatics (for rare cancer research) to Dr Justin Bedo, who works with Associate Professor Tony Papenfuss.

Dr Barker and Dr Bedo will be using molecular and genomic technologies to pinpoint critical genes that drive rare cancers.

Associate Professor Scott said a major objective of this research was to recommend effective treatments for rare cancer patients using existing anti-cancer medications and new targeted therapies.

"Once a treatment for a rare cancer patient is devised, our researchers would monitor the success of the treatment and this information would guide future recommendations," she said.

Support from the Stafford Fox Medical Research Foundation is enabling research that aims to match rare cancer patients with existing anti-cancer medications.

The funding has supported the appointment of Dr Holly Barker (right) as the Stafford Fox Centenary Fellow in rare cancer research, and Dr Justin Bedo (left) as the Stafford Fox Centenary Fellow in bioinformatics (for rare cancer research), pictured with foundation trustee Mr Ken Wallace (centre left) and Mrs Marian Wallace.

Photo credit: Casamento Photography

MOLECULAR GENETICS OF CANCER

The Molecular Genetics of Cancer division is investigating how our cells normally die and how defects in this process cause disease, particularly cancer.

A better understanding of cell death will help us to develop improved treatments for both cancers and immune disorders.

Targetting necroptosis in inflammatory diseases

A form of regulated cell death known as necroptosis has recently been implicated in severe inflammatory conditions including pancreatitis and inflammatory bowel disease.

Dr Silvia Alvarez-Diaz has led research defining the important and different roles played by two proteins, MLKL and RIPK3, in regulating necroptosis, using a preclinical model of an autoimmune disease.

The research indicated that potential new drugs that specifically target MLKL or RIPK3 could be used to boost or repress necroptosis. As such they may have future applications in the treatment of a range of conditions, including inflammatory and autoimmune diseases, and cancer.

Quality control in T cell development

T cells are an important component of the immune system, orchestrating immune responses in reaction to infections. The thymus acts as a 'school' for developing T cells, training them how to fight infections and eliminating those cells that have the potential to launch dangerous autoimmune attacks on the body's own tissues.

Dr Charis Teh, Dr Daniel Gray and collaborators have discovered a previously unrecognised 'quality control' step within the thymus that may protect against autoimmune diseases such as type 1 diabetes and multiple sclerosis. The team discovered that a protein complex called LUBAC was important for a very late stage of thymic T cell development. This finding may have future therapeutic applications for treating autoimmune diseases.

International awards for cell death research

Scientists in the division were recognised by international organisations for their research achievements in understanding of the role of cell death in health and disease.

The Rockefeller University, US, awarded an honorary Doctor of Science degree to Professor Suzanne Cory AC for her career contributions to advancing immunology and cancer biology.

Professor Andreas Strasser was awarded the European Cell Death Organization Career Award in recognition of his achievements over three decades in the field. During this time Professor Strasser has led investigations of how cell death is controlled at the molecular level, and how it impacts cancer and immune disorders.

Health impact

Cancers: leukaemia, lymphoma, myeloma, myeloproliferative disorders, stomach cancer

Immune disorders: lupus, rheumatoid arthritis, type 1 diabetes

Other areas: personalised medicine

Division heads

Professor Jerry Adams

Professor Andreas Strasser

Laboratory heads

Dr Philippe Bouillet

Professor Suzanne Cory
(honorary distinguished research fellow)

Dr Daniel Gray

Dr Marco Herold

Dr Ruth Kluck

46 publications

44 staff
11 students
3 clinicians

Targetable vulnerability revealed in blood cancers

Seventy per cent of cancers have abnormally high levels of a protein called MYC, which forces cells into unusually rapid growth.

Institute researchers have discovered a missing piece in the puzzle of understanding how high levels of MYC drive cancer development, opening the door for potential future treatments or even prevention of these cancers.

Dr Stephanie Grabow, Dr Brandon Aubrey, Professor Andreas Strasser and colleagues discovered that the development of blood cancers driven by MYC could be prevented by lowering the levels of another protein, called MCL-1.

Dr Grabow said MCL-1 was a protein that kept stressed cells, such as those in the process of becoming cancerous, alive by preventing programmed cell death. "No-one had realised just how vulnerable cells undergoing cancerous changes are to a relatively minor reduction in the levels of MCL-1," Dr Grabow said.

"NO-ONE HAD REALISED JUST HOW VULNERABLE CELLS UNDERGOING CANCEROUS CHANGES ARE TO A RELATIVELY MINOR REDUCTION IN THE LEVELS OF MCL-1"

"We found that MCL-1 is critical for keeping developing cancer cells alive through the stressful events that are associated with the transformation of a healthy cell into a cancerous cell."

The result is particularly exciting because MCL-1 inhibitors are already in development as anti-cancer drugs.

Institute researchers, working with colleagues at The Alfred Hospital and the international pharmaceutical company Servier, showed that targetting MCL-1 with a compound called S63845 was effective and tolerable in targetting several cancer types, including lymphomas driven by the protein MYC.

S63845 was developed jointly by Servier, headquartered in France, and Vernalis (R&D), a company based in the UK.

PhD student Dr Aubrey, who is also a clinical haematologist at The Royal Melbourne Hospital, said that as well as providing insights into better treatments for MYC-driven cancers, the research could also inform future strategies to prevent cancer from forming in the first place.

"Cancer researchers are building a better picture of who is at risk of developing cancer, and enhancing how we can detect early stage cancer in people before it has grown to the point of causing illness," Dr Aubrey said.

"Early treatment or even prevention of cancer is likely to be a more effective way to fight cancer than treating an established cancer after it has already formed and made a person sick.

"This research has suggested that, in the future, MCL-1 inhibitors might have potential benefit for treating MYC-driven cancers, even at very early stages," Dr Aubrey said.

Collaborating divisions

Molecular Genetics of Cancer, ACRF Chemical Biology, Cancer and Haematology

Collaborating organisations

The Alfred Hospital, Monash University, The Royal Melbourne Hospital, Servier (France), the University of Melbourne

Funding partners

Australian Cancer Research Foundation, Australian Department of Education and Training, Australian National Health and Medical Research Council, Cancer Council Victoria, Cancer Therapeutics Cooperative Research Centre, Kay Kendall Leukemia Fund (UK), the Lady Tata Memorial Trust (UK), the Leukemia and Lymphoma Society (US), the Leukaemia Foundation of Australia, the estate of Anthony (Toni) Redstone OAM, Servier (France), the University of Melbourne, Victorian Cancer Agency, Victorian Government Operational Infrastructure Support Program

More information

Grabow S *et al*. Loss of a single *Mcl-1* allele inhibits MYC-driven lymphomagenesis by sensitizing pro-B cells to apoptosis. *Cell Reports*. 2016 Mar 15;14(10):2337-47

Kotschy A *et al*. The MCL1 inhibitor S63845 is tolerable and effective in diverse cancer models. *Nature*. 2016 Oct 27;538(7626):477-482

High levels of the protein MYC are found in more than half of all cancers. Dr Stephanie Grabow and colleagues have revealed that the cell survival protein MCL-1 is an Achilles' heel of MYC-driven cancers, and could be a future therapeutic target.

Long-term support underpins leukaemia research program

Since 2001 the Institute has hosted a Specialized Center of Research (SCOR) funded by the US-based Leukemia & Lymphoma Society.

More than $20 million in support through this program has enabled a team of researchers at the Institute to pursue a long-term program that has revealed how cell survival is controlled in healthy and cancerous cells. Their discoveries have underpinned the development of a new class of anti-cancer drugs now available to treat some forms of leukaemia.

"THE GENEROUS AND LONG-TERM SUPPORT FROM THE LEUKEMIA & LYMPHOMA SOCIETY HAS ENABLED US TO PURSUE OUR VISION OF BASIC RESEARCH UNDERPINNING NEW THERAPIES FOR CANCER"

Professor Jerry Adams, who leads the SCOR, said the team's research was based on an important insight made by Institute researchers in 1988. "We discovered that impaired cell death can contribute to the development of cancer and limit its treatment," he said. "The generous and long-term support from the Leukemia & Lymphoma Society has enabled us to pursue our vision of basic research underpinning new therapies for cancer."

A collaboration between the Institute and US pharmaceutical companies AbbVie and Genentech, a member of the Roche group, led to the co-development of a new anti-cancer agent, venetoclax. This drug inhibits the protein BCL-2, the same molecule that Institute researchers had first implicated in boosting the survival of cancer cells.

Following the outcomes of clinical trials of the inhibitor that involved Institute clinician-scientists, venetoclax has now been approved in Australia, the US and the European Union for the treatment of certain high-risk forms of chronic lymphocytic leukaemia, a common leukaemia in adults.

Dr Lee Greenberger, who oversees the Leukemia & Lymphoma Society's SCOR program, said that the program aimed to enhance interdisciplinary research among its participants in order to discover new approaches to treating patients with blood cancers.

"The Walter and Eliza Hall Institute's SCOR is one of the society's longest running grant programs," he said. "We are very gratified that our support of this SCOR has contributed to discoveries that underpinned the development of a new treatment for people with CLL. Notably, it is the longest running Leukemia & Lymphoma Society SCOR program that has translated basic laboratory research into a newly approved therapy."

Professor Adams said that SCOR scientists were continuing to work towards new approaches that exploit the cell death machinery to better treat blood cancers. "New therapies are desperately needed for many forms of leukaemia and lymphoma", he said. "We hope that our research will contribute to better treatments for many people around the world suffering from these diseases."

Since 2001 Professor Jerry Adams has led a Specialized Center of Research at the Institute funded by the US-based Leukemia & Lymphoma Society.

ACRF CHEMICAL BIOLOGY

The ACRF Chemical Biology division investigates key biological processes and pathways critical in disease development to discover potential drug targets important for human disease.

Our researchers use chemical, biochemical, structural and biological approaches to establish how dysregulation of critical cell signalling pathways contributes to disease, and use this to guide novel therapeutic development.

Promising new anti-cancer target

For the first time, Institute researchers working in collaboration with The Alfred Hospital and international pharmaceutical company Servier have obtained clear preclinical evidence that inhibiting the cell survival protein MCL-1 was effective in targetting several cancer types.

MCL-1 is a protein that prevents programmed cell death, and has been implicated in sustaining the growth of up to a quarter of all cancers. The research presents a new way to efficiently kill cancerous cells and holds promise for the treatment of blood cancers such as acute myeloid leukaemia, lymphoma and multiple myeloma, as well as solid cancers such as melanoma and cancers of the lung and breast. The finding was made using a new compound, S63845, that was discovered jointly by Servier and Vernalis (R&D), a UK-based company.

First 3D map of cell-building protein

Institute researchers have used the Australian Synchrotron to reveal the three-dimensional molecular 'map' of the protein DCLK1, which has been proposed as a driver of many types of cancers. The unprecedented view of the protein could provide clues to how it contributes to cancer formation and progression.

Dr Onisha Patel and Dr Isabelle Lucet, in collaboration with scientists at the Olivia Newton-John Cancer Research Institute, pinpointed the parts of DCLK1 that can malfunction in cancer cells, providing new information about how the protein functions. The discovery may also be the first step towards designing a drug that precisely targets DCLK1, with potential applications as an anti-cancer treatment.

Eureka Prize for groundbreaking cancer discovery

Research that led to the development of the new anti-cancer drug, venetoclax, was awarded the 2016 Johnson & Johnson Eureka Prize for Innovation in Medical Research.

Venetoclax is a so-called BH3-mimetic drug that kills cancer cells by switching off the cell's in-built survival machinery. It was co-developed for clinical use by international pharmaceutical companies AbbVie and Genentech, a member of the Roche group. Venetoclax has been approved for the treatment of certain high-risk forms of leukaemia in Australia, the US and the European Union.

The award presented to Associate Professor Guillaume Lessene, Professor David Huang, Dr Peter Czabotar and Professor Andrew Roberts recognised their role in the team that developed venetoclax and other BH3-mimetic agents.

Health impact

Cancers: blood cancer, breast cancer, myeloproliferative disease, stomach cancer

Immune disorders: Crohn's disease, inflammatory bowel disease, psoriasis, rheumatic fever and heart disease

Infectious diseases: HIV, malaria, toxoplasmosis

Other areas: heart disease and stroke, neurodegenerative disease, thalassemia

Division heads

Professor Benjamin Kile

Associate Professor Guillaume Lessene

Laboratory heads

Associate Professor Chris Burns, visiting scientist

Dr Ethan Goddard-Borger

Dr Isabelle Lucet

Professor Keith Watson, honorary

37 publications

32 staff

14 students

Dr Ethan Goddard-Borger (right) and Professor Spencer Williams (Bio21 Institute and The University of Melbourne) discovered the enzyme that microorganisms use to digest an unusual sugar molecule found in green vegetables. Their research may lead to therapies that promote the growth of beneficial bacteria, as well as potentially underpinning the development of new antibiotics.

Sweet discovery in leafy greens holds key to gut health

A discovery about how bacteria feed on an unusual sugar molecule found in green vegetables could hold the key to the development of new 'prebiotic' therapies that support the growth of beneficial bacteria, protecting our gut and promoting gastrointestinal health.

Dr Ethan Goddard-Borger, collaborating with Professor Spencer Williams from the Bio21 Institute and The University of Melbourne, and Professor Gideon Davies from the University of York, UK, identified a previously unknown enzyme, YihQ, that is used by bacteria, fungi and other organisms to feed on the unusual but abundant sugar sulfoquinovose – SQ for short – that is found in green vegetables such as spinach.

"WE HOPE OUR DISCOVERY COULD BE EXPLOITED TO CULTIVATE THE GROWTH OF GOOD GUT BACTERIA"

The research suggests that the SQ sugars in leafy greens are essential for feeding 'good' gut bacteria, which form a protective barrier that limits the growth of harmful bacteria, while also nourishing the human cells lining the colon and modulating the immune system.

"Each year, photosynthetic organisms, including leafy green plants, produce SQ sugars on an enormous scale globally, comparable to the world's total annual iron ore production," Dr Goddard-Borger said.

Every time we eat green vegetables we consume significant amounts of SQ sugars, which are used as an energy source by good gut bacteria.

"We speculate that consumption of this specific molecule within leafy greens will prove to be an important factor in improving and maintaining healthy gut bacteria and good digestive health. We hope our discovery could be exploited to cultivate the growth of good gut bacteria," Dr Goddard-Borger said.

The discovery also provides crucial insights that may one day underpin the development of an entirely new class of antibiotics.

"New antimicrobial strategies are desperately needed as more and more bacteria acquire resistance to existing antibiotics," Dr Goddard-Borger said.

"We think it will be possible to use these widespread enzymes to enable highly specific delivery of antibiotics to harmful forms of *E. coli* and other pathogens such as *Salmonella*, responsible for food poisoning, while leaving beneficial gut bacteria untouched," he said.

Collaborating organisations

Bio21 Molecular Science and Biotechnology Institute, the University of Melbourne, University of York (UK)

Funding partners

Australian Cancer Research Foundation, Australian National Health and Medical Research Council, Australian Research Council, European Research Council Ramaciotti Foundation, UK Biotechnology and Biological Sciences Research Council, veski, the Victorian Government Operational Infrastructure Support Program

More information

Speciale G *et al*. YihQ is a sulfoquinovosidase that cleaves sulfoquinovosyl diacylglyceride sulfolipids. *Nature Chemical Biology*. 2016 Apr;12(4):215-7

Donation helps to bridge the ‘valley of death’ for a potential new cancer drug

Considerable effort worldwide – including at the Institute – has helped to unravel many of the complex biological processes that drive diseases. The challenge for today’s medical researchers is to take these findings and translate them into better treatments for these diseases – a pathway that involves drug discovery, development and preclinical validation, followed by clinical trials.

This pathway of translation towards the clinic is expensive. At each stage of development, there is the risk that the journey will not lead to a successful new therapy.

> “ONCE WE KNOW HOW THE DRUG WORKS, WE WILL BE ABLE TO EXPLAIN BETTER WHY THE DRUG CAN STOP CANCER GROWTH”

Medicinal chemist Associate Professor Guillaume Lessene says the risks of drug discovery and preclinical validation can deter biotech and pharmaceutical companies from investing in entirely novel areas.

“Unfortunately, the high cost limits the ability of not-for-profit and academic research programs to undertake this research without an industry partner,” he said. “We are also limited in the government funding that we can access for this type of research. The gap in funding for drug discovery and validation has led to this research being referred to as the ‘valley of death’.”

Associate Professor Lessene’s research into a new cancer treatment was nearly stopped by the valley of death: his team had discovered a new drug that showed considerable promise as a new treatment for people with cancer, but could not fund the next stage of research.

It was at this point that an anonymous donor decided to help this project continue. They have provided funding that will enable 12 months of further research on the potential new drug.

This time will enable Associate Professor Lessene and collaborators at the Institute to investigate the potency of the new drug for blocking cancer growth.

“The additional time will also allow us to make the link between the new drug and its target inside the cancer cell, a process called ‘target identification’,” Associate Professor Lessene said. “Once we know how the drug works, we will be able to explain better why the drug can stop cancer growth.”

With this information to hand, the next stage will be to progress the drug to early phase drug development, and potentially seek a commercial partner that may fund clinical trials.

“We are extremely grateful for the generosity of this donor, who has enabled an exciting project to continue, which we hope will one day benefit people with cancer,” Associate Professor Lessene said.

Dr Isabelle Lucet (left) and Dr Onisha Patel revealed the three-dimensional molecular ‘map’ of the DCLK1 protein, which could provide clues to how DCLK1 contributes to cancer formation and progression.

MOLECULAR MEDICINE

The Molecular Medicine division investigates how biological systems function and are controlled in normal and disease states.

With programs focused on blood cell production and function, epigenetics and cancer, our goal is to pinpoint molecular targets for disease diagnosis and treatment.

New clue in X chromosome inactivation

Female mammals have two copies of the X chromosome, while males have only one. Early in the development of a female embryo, one copy of the X chromosome is silenced in each cell – a process known as 'X inactivation'.

X inactivation involves 'epigenetic' changes to the chromosome's DNA that make the genes on it inaccessible, or 'silent'. A research team led by Associate Professor Marnie Blewitt, Dr Matthew Ritchie and Professor Doug Hilton has investigated the nature of these epigenetic changes.

The team revealed a protein called Setdb1 is important for silencing genes on the X chromosome. Their finding also resolved a longstanding controversy by demonstrating that a particular epigenetic silencing process called 'histone 3 lysine 9 methylation' occurred during X inactivation.

NHMRC support to improve blood therapies

The production of the diverse cells of the blood is a critical process that occurs throughout our lives.

Funding from the National Health and Medical Research Council (NHMRC) is enabling Dr Samir Taoudi to undertake research into how blood develops from stem cells within the body, and investigate how this can be mimicked in laboratory-based blood production systems. It is hoped that in the future laboratory-produced blood could be used as a sustainable alternative to donor blood transfusions for people whose own blood forming systems have failed.

Dr Taoudi's team is also investigating the differences in blood functions between children and adults, with a goal of informing the tailoring of blood product therapies for children with blood disorders.

Benchmarking gene expression

While different cells within our body contain the same genetic sequence – their genome – they differ in which genes are being used in each cell type at a certain time.

'Transcriptome profiling' is a collective name for methods that provide information about which genes are active in a particular sample, or compare the activity of genes under different conditions, for instance, in healthy or diseased states. In recent times a method called RNA-seq has gained popularity for transcriptome profiling.

Dr Aliaksei Holik, Dr Charity Law and Dr Matthew Ritchie have generated a novel dataset that allows for systematic comparison of the quality of different protocols and analytical tools used for RNA-seq. This will allow researchers to make clearer choices when selecting the right protocol or analytical tool for their studies.

Health impact

Cancers: blood cancer, leukaemia

Immune disorders: allergy, asthma, multiple sclerosis, rheumatoid arthritis

Other areas: epigenetics, facioscapulohumeral muscular dystrophy, personalised medicine, regenerative medicine

Division head

Professor Doug Hilton

Laboratory heads

Associate Professor Marnie Blewitt

Dr Shalin Naik

Dr Matthew Ritchie

Dr Samir Taoudi

Professor Christine Wells

25 publications

38 staff

14 students

1 clinician

Online ‘atlas’ of blood cells to help target disease cures

The cells in our blood hold clues to many aspects of human health and disease.

Blood cells are at the root of diseases such as leukaemia, autoimmune and inflammatory diseases. They are also essential in responding to our bodies needs, such as after metabolic changes or a reduction in oxygen.

Institute researchers have developed a new online database known as Haemopaedia, which maps the expression of 20,000 genes in 54 different blood cell types.

Referred to as the ‘Wikipedia’ of blood cells, Haemopaedia allows users to access, analyse and cross-reference their research data and is freely available to the public as well as the scientific community.

“THIS RESOURCE WILL HELP SCIENTISTS ACROSS THE WORLD TO DISCOVER PATTERNS OF GENE EXPRESSION THAT SHOW HOW PARTICULAR CELLS MAY BE TARGETED BY DRUGS”

Dr Carolyn de Graaf, who led the research team that developed Haemopaedia, said the team hoped to improve the global research community’s understanding of the molecular and genetic regulation of blood cell function and production.

“This resource will help scientists across the world to discover patterns of gene expression that show how particular cells may be targeted by drugs,” Dr de Graaf said.

Haemopaedia is supported by a web portal called Haemosphere, that was developed by Dr Jarny Choi.

Dr Choi said large datasets such as Haemopedia were often difficult to navigate. “Having a set of easy-to-use online tools aimed at a diverse range of researchers in the field adds enormous value to the resource,” he said.

Collaborating divisions

Molecular Medicine, Bioinformatics, Cancer and Haematology, Immunology, Molecular Immunology

Collaborating organisations

CSIRO Manufacturing, CSL, Monash University, Tsinghua University (China), the University of Melbourne

Funding partners

Australian National Health and Medical Research Council, Cancer Council Victoria, CSL, Science and Industry Endowment Fund, Victorian Government Operational Infrastructure Support Program

More information

de Graaf CA *et al*. Haemopedia: an expression atlas of murine hematopoietic cells. *Stem Cell Reports*. 2016 Sep 13;7(3):571-82

Transfusions of blood stem cells are used to treat people whose own blood forming systems have failed.

In 2016 Dr Samir Taoudi received more than $1 million in funding from the National Health and Medical Research Council to investigate how blood is formed in adults and children, and how blood therapies could be improved.

Gene discovery could lead to muscular dystrophy treatment

Facioscapulohumeral muscular dystrophy (FSHD) is an inherited progressive muscle-wasting disease affecting the face, arms and shoulders. No treatments are available for this debilitating disease, which is most commonly diagnosed in teenagers and young adults.

The FSHD Global Research Foundation is supporting Associate Professor Marnie Blewitt, Dr James Murphy and Associate Professor Chris Burns to develop new medicines that could halt the progression of FSHD.

Following international research identifying mutations in SMCHD1 as the cause of one form of FSHD, called FSHD2, Associate Professor Blewitt, Dr Murphy and Dr Kelan Chen showed how the mutations disabled SMCHD1's function.

> "WE ARE THRILLED TO BE FUNDING THIS PROMISING AREA OF RESEARCH AT THE WALTER AND ELIZA HALL INSTITUTE"

In another form of FSHD, called FSHD1, mutations in SMCHD1 result in more severe disease. Associate Professor Blewitt said her team showed that these mutations disabled SMCHD1's ability to act as an epigenetic suppressor – a protein that binds DNA to switch off genes unnecessary for a particular cell's function.

"In people with FSHD2, a small change in SMCHD1 is enough to stop it from binding to the DNA properly, and prevent it from doing its job," Associate Professor Blewitt said.

In 2016, the team discovered that mutations in SMCHD1 also caused a rare syndrome called bosma arhinia microphthalmia syndrome (BAMS), in which a baby's nose fails to form during embryonic development.

"We were amazed to discover that BAMS occurs when SMCHD1 is activated inappropriately – the opposite of what is happening in FSHD2," Associate Professor Blewitt said. "This discovery is really exciting because it gives us clues about how to design medicines that boost SMCHD1's activity to correct the defect that causes FSHD."

With a grant from the FSHD Global Research Foundation the team will search for chemicals that can boost SMCHD1 function, by screening a library of 120,000 drug-like molecules. Promising molecules can then be refined to develop potential drugs that might treat FSHD.

Ms Natalie Livet, CEO of FSHD Global Research Foundation, said the foundation was committed to advancing medical research and education into FSHD to find treatments, and ultimately a cure, for the debilitating disease.

"We are thrilled to be funding this promising area of research at the Walter and Eliza Hall Institute," Ms Livet said. "Our hope is that it will lead to new therapies that could either halt the progression of FSHD, or potentially improve symptoms or even prevent the disease in people at genetic risk."

Facioscapulohumeral muscular dystrophy (FSHD) is an inherited and incurable muscle-wasting disease. A grant from the FSHD Global Research Foundation is enabling Dr James Murphy (left), Dr Kelan Chen (centre) and Associate Professor Marnie Blewitt to develop new medicines that could halt the progression of FSHD.

STRUCTURAL BIOLOGY

The Structural Biology division is interested in discovering new medicines through studies of the three-dimensional structure of large biological molecules that are either targets for drugs or potential therapeutic agents.

New approaches for treating resistant bowel cancers

People with metastatic bowel cancer often respond poorly to available treatments. Professor Tony Burgess' research into new treatments for chemotherapy-resistant bowel cancers has received funding from AUSiMED (Australia Israel Medical Research), matching a VISITS Victorian Government grant.

The funding has enabled Professor Burgess to collaborate with Professor Alex Levitzki at Hebrew University, Israel. Their research is investigating malignant bowel cancers that are driven in part by a protein called EGFR. Although there are treatments available that target EGFR, they only help 50 per cent of bowel cancer patients. Professor Burgess and Professor Levitzki's research is investigating new anti-cancer drug combinations aimed at improving the efficacy of targetting EGFR to treat bowel cancers.

New insights into electrical signalling

The pumping of the heart is controlled by electrical impulses and, when these do not work correctly, heart rhythm problems called arrhythmias can arise.

Dr Jacqui Gulbis and Dr David Miller are investigating the proteins that mediate electrical signalling within the body, to understand how defects in these proteins cause heart arrhythmias and other diseases.

A grant from the Joe White Bequest has enabled the purchase of highly sensitive equipment that Dr Gulbis and Dr Miller are using to measure electrical activity across cell membranes. By understanding how the proteins turn electrical currents on and off, the team aim to discover how to modulate their activity as a new approach to treating a broad spectrum of diseases.

'Organoid bank' to improve pancreatic cancer therapies

Funding from the Avner Pancreatic Cancer Foundation has enabled the establishment of Australia's first pancreatic cancer 'organoids bank' in a project jointly led by Dr Tracy Putoczki, Professor Tony Burgess, Associate Professor Peter Gibbs and Dr Belinda Lee at the Institute, with Professor Sean Grimmond at the University of Melbourne.

The organoid bank will consist of thousands of pieces of living pancreatic tissue grown from each pancreatic cancer patient. Each organoid is the size of a grain of sand and can be used to compare the efficacy of up to 15 anti-cancer drug combinations. The results will be used to rapidly predict which drug combinations are likely to provide the most effective treatment for each pancreatic cancer patient.

Health impact

Cancers: bowel cancer, brain cancer, leukaemia, lymphoma, myeloma, myeloproliferative disorders

Immune disorders: type 1 diabetes, type 2 diabetes

Infectious disease: malaria

Other areas: heart disease and stroke, neurodegenerative disease

Division head

Professor Peter Colman

Laboratory heads

Dr Jeff Babon
Professor Antony Burgess
Dr Matthew Call
Dr Melissa Call
Dr Peter Czabotar
Dr Jacqui Gulbis
Associate Professor Mike Lawrence
Dr Isabelle Lucet
Dr Colin Ward, associate research fellow

33 publications

37 staff
12 students
3 clinicians

Insulin treatment is vital for controlling blood glucose levels for most people with type 1 diabetes, and some people with type 2 diabetes.

An insulin-like protein found in the venom of the marine cone snail could hold the clue to better insulin treatments, according to research by Associate Professor Mike Lawrence and colleagues.

Cone snail venom could improve diabetes treatments

Treatment with insulin is essential for most people with type 1 diabetes, and some people with type 2 diabetes, to control the levels of glucose in their blood.

Poor control of blood glucose can lead to serious health complications including eye disease, kidney disease, nerve damage and heart disease.

A study of an insulin-like protein found in the venom of the marine cone snail *(Conus geographus)* could hold the clue to better insulin treatments.

Cone snails use their venom to trap their prey. When fish are exposed to the venom, they immediately become immobilised by a drop in their blood glucose level that is induced by an insulin component within the venom.

"WE HOPE THAT WE WILL BE ABLE TO SEE NEW, ULTRA-FAST-ACTING FORMS OF INSULIN DEVELOPED"

Working with an international team of collaborators, Associate Professor Mike Lawrence used the Australian Synchrotron to determine the three-dimensional atomic structure of the cone snail venom insulin, which has led to an understanding of how the venom insulin has such a rapid effect.

Associate Professor Lawrence said the cone snail venom insulin, called Con-Ins G1, was able to avoid the structural changes human insulin must undergo to activate.

"We found that cone snail venom insulins are primed and ready to bind to their receptors on cells with no further activation," Associate Professor Lawrence said.

"By comparison, human insulins can be considered 'clunky': their structure contains an extra hinge-like component that has to open before any connection between insulin and its receptor can take place.

"Our study of the cone snail venom insulin has revealed how we could remove the hinge from human insulin and thus enable it to take effect more rapidly as a therapeutic."

The international research team also showed that the cone snail venom insulin is able to bind to human insulin receptors, strengthening the view that the research may have the potential to inform new human therapeutics.

"Cone snail venom insulin can 'switch on' human insulin cell signalling pathways by successfully binding to human receptors," Associate Professor Lawrence said. "We hope that we will be able to see new, ultra-fast-acting forms of insulin developed, and work to implement this has already begun."

Collaborating organisations

Flinders University, La Trobe University, Monash Institute of Pharmaceutical Sciences, Sentia Medical Sciences (US), University of Utah (US)

Funding partners

Australian National Health and Medical Research Council, European Commission, National Institutes of Health (US), University of Utah (US), Utah Science Technology and Research Initiative (US), Victorian Government Operational Infrastructure Support Program

More information

Menting JG *et al*. A minimized human insulin-receptor-binding motif revealed in a *Conus geographus* venom insulin. *Nature Structural and Molecular Biology*. 2016 Oct;23(10):916-920

Combination therapies may improve outcomes for people with brain cancer

More than 1600 Australians are diagnosed with brain cancer each year, and fewer than 20 per cent are alive five years after their diagnosis.

Unfortunately there has been little improvement in survival rates over the past 30 years, despite brain cancer causing more deaths in people under the age of 40 than any other cancer – and causing more deaths in Australian children than any other disease.

"I'VE WATCHED MY COLLEAGUES WORKING WITH OTHER CANCERS FIND NEW DRUGS AND APPROACHES, CHANGING THE FUTURE FOR THEIR PATIENTS, AND I WANT TO SEE THAT FOR MY PATIENTS. THIS GRANT TAKES US A STEP CLOSER"

Dr Ruth Mitchell is a trainee neurosurgeon at the Royal Melbourne Hospital and PhD student at the Institute. Her research focuses on glioblastoma multiforme (GBM), the most common and aggressive form of brain cancer.

A research grant from the Brain Foundation, Australia's largest independent funder of brain research, is enabling Dr Mitchell to focus her research on a protein called epidermal growth factor receptor (EGFR).

EGFR is found on the surface of many normal cell types, but in brain cancer cells it can be overactive and mutated, which causes the cancer to grow. In the past decade new medicines that block EGFR have showed promise for improving the outcomes of people with certain cancers.

Dr Mitchell said her research could lead to new combination therapies for people with GBM that improve their chances of survival.

"I've seen first-hand the devastating impact this cancer has on the lives of my patients and their families," Dr Mitchell said.

"I've watched my colleagues working with other cancers find new drugs and approaches, changing the future for their patients, and I want to see that for my patients. This grant takes us a step closer."

The Secretary General of the Brain Foundation Mr Gerald Edmunds said research was the pathway to recovery and prevention.

"I am delighted that we are supporting Dr Ruth Mitchell's important research into brain cancer," Mr Edmunds said. "We look forward to ongoing collaborations with the Institute into the future, to ensure the success of this exciting research.

Dr Mitchell's PhD studies are supported by a scholarship from Royal Australasian College of Surgeons.

A grant from Australia's Brain Foundation is enabling Dr Ruth Mitchell (left) to investigate new approaches to treating a common and deadly form of brain cancer. Dr Mitchell is pictured with Brain Foundation Secretary General Mr Gerald Edmunds.

BIOINFORMATICS

The Bioinformatics division collaborates with Institute and external researchers in designing, conducting and analysing genomic and molecular sequence studies to understand biology and disease. We also conduct research to improve existing methods and develop novel methods for analysing data.

Cancer research excellence award

PhD student Mr Daniel Cameron won a 2016 Picchi Award for Excellence in Cancer Research, which recognises the productivity and impact of cancer research by students at Victorian Comprehensive Cancer Centre partners.

Mr Cameron, who is supervised by Associate Professor Tony Papenfuss, has developed innovative new algorithms to improve the detection of genomic rearrangements in cancer using sequencing. Genomic rearrangements are an important type of mutation in cancer. As part of his PhD, Mr Cameron developed an award-winning software program GRIDSS (Genome Rearrangement Identification Software Suite), a powerful new approach to detecting these rearrangements. GRIDSS is already in use on patient samples.

Improving gene expression analyses

Much of the variation between the cells in our body can be attributed to changes in the genes that are expressed in the cells. Detecting changes in gene expression is one of the most common tasks in statistical analysis of genomic data, but the resultant data can be complex to interpret.

Professor Gordon Smyth, with Dr Belinda Phipson from the Murdoch Children's Research Institute, discovered how a widely-used statistical technique could be improved for analysing gene expression. Their new method makes statistical tests more powerful and robust when some of the genes in the samples show high uncertainty, enabling the user to detect more gene changes likely to be scientifically relevant.

Pinpointing aggressive cancers

Cancer metastasis, in which cancer cells disperse throughout the body, is the leading cause of death from solid tumours.

The cell signalling protein transforming growth factor-β (TGF-β) is known to cause changes in cancer cells that promotes metastasis. Dr Melissa Davis, PhD student Ms Momeneh Foroutan and colleagues used computational biology to analyse the genes expressed in a large collection of cancer cell lines and patient samples.

They identified a 'signature' of gene changes that identifies tumours with aggressive, TGF-β-driven behaviour. In the future this may be used to identify cancers that would respond favourably to therapies that inhibit TGF-β.

Health impact

Cancers: bowel cancer, breast cancer, leukaemia, lung cancer, lymphoma, myeloma, ovarian cancer, rare cancers, stomach cancer

Immune disorders: acute rheumatic fever, lupus, multiple sclerosis, rheumatoid arthritis, thyroid orbitopathy, transplantation, type 1 diabetes

Infectious diseases: malaria, scabies, tuberculosis, toxoplasmosis

Other areas: congenital disease, Down syndrome, heart disease and stroke, neurodegenerative disease, personalised medicine

Division head

Professor Gordon Smyth

Laboratory heads

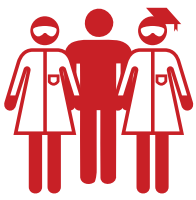
Dr Melissa Davis

Associate Professor Tony Papenfuss

Dr Wei Shi

Professor Terry Speed

55 publications



41 staff

23 students

Making sense of complex biological data

The differences between healthy and diseased tissues are attributable to changes in proteins and genes.

Modern approaches to detecting these changes can generate huge and complex sets of data. The Institute's bioinformatics researchers are developing novel and sophisticated approaches to analysing and understanding these data.

Professor Terry Speed and colleagues at the University of Lyon, France, and the University of California, Berkeley, US, have improved how variation that is unrelated to a biological process can be removed from experimental data.

Many experiments, even those that are optimally designed, contain unwanted variation that complicates the data analysis, Professor Speed said.

"FLAWED DATA ANALYSIS IS A PITFALL OF RESEARCH USING HIGH-THROUGHPUT TECHNOLOGIES"

"We know that many sources of variation can exist, even down to two batches of the same reagent producing different results, when looking at gene expression in a sample," he said.

"Today's high-throughput technologies, in which thousands of genes or proteins may be analysed in hundreds or thousands of samples, mean that even subtle sources of variation have the potential to cause 'false positives' – where a change is detected that doesn't exist – or 'false negatives' – where a change exists but can't be detected," Professor Speed said.

More than a decade ago Professor Speed became involved in research examining changes in gene expression in the brains of people with psychiatric conditions.

"The brain is a particularly challenging tissue to study, and the added complexity of studying human post-mortem samples meant that there were artifacts impeding the correct interpretation of the data," he said. "That study was a starting point for my colleagues and I to develop statistical techniques that have now been applied to other fields of medical research.

"We now have a system that enables researchers to utilise 'negative control' genes, that should be relatively stable, and 'positive controls' that should change in known ways in the experimental situation, and replicate samples, in order to identify and remove unwanted variation between samples," Professor Speed said.

One aspect of the research has been to develop a free software program, RUVnormalize, which removes unwanted variation from gene expression data sets.

"Flawed data analysis is a pitfall of research using high-throughput technologies," Professor Speed said. "As much time and money is wasted in pursuing unintentionally false findings as is wasted in conducting experiments that have uninterpretable results. We have seen time and again that using statistical bioinformatics to make sense of complex data can make a huge difference in medical research."

Collaborating organisations

University of Lyon (France), University of California, Berkeley (US)

Funding partners

Australian National Health and Medical Research Council, Stand Up to Cancer, Victorian Government Operational Infrastructure Support Program

More information

Jacob L *et al*. Correcting gene expression data when neither the unwanted variation nor the factor of interest are observed. *Biostatistics*. 2016 Jan;17(1):16-28

High-throughput experimental technologies generate large sets of data that can contain unwanted variation that complicates the data analysis.

Bioinformatics researcher Professor Terry Speed and international collaborators have developed a new approach that allows variation that is unrelated to a biological process to be removed from experimental data.

Genomics sheds light on parasite

More than half of children living in remote Aboriginal communities are infected with scabies each year. This skin parasite causes intense itching and predisposes carriers to bacterial infections that cause serious lifelong or fatal illnesses including rheumatic fever and subsequent rheumatic heart disease, and kidney disease.

Associate Professor Tony Papenfuss is using genomic technologies to understand the scabies mite's genetic makeup, with the goal of revealing vulnerabilities that could improve scabies prevention and treatment.

"WE HOPE THAT IN THE LONG TERM THIS INFORMATION WILL UNDERPIN NEW STRATEGIES TO PREVENT AND TREAT SCABIES INFESTATIONS, AND PREVENT LIFELONG COMPLICATIONS FOR PEOPLE IN REMOTE ABORIGINAL COMMUNITIES"

This research has been boosted by new genomic sequencing and analytical tools made possible by funding from the Scobie and Claire Mackinnon Trust and the Lettisier Foundation.

Genomic technologies are critical for finding ways to prevent and control scabies, Associate Professor Papenfuss said. "A shocking seven out of 10 children in remote Aboriginal communities will contract scabies before they reach one year of age," he said.

"Many diseases have benefited from the genomics revolution taking place in medicine – most notably cancer. We are excited that we can now apply these technologies to tackle a major, yet neglected, health problem in Aboriginal Australians."

Associate Professor Papenfuss' team, working with collaborators at QIMR Berghofer Medical Research Institute and the Menzies School of Health Research, revealed the first genetic 'map' of the human scabies mite in 2016.

"Understanding the genetic makeup of the scabies mite will help to identify how the parasite becomes resistant to certain drugs and could suggest new strategies for the development of novel therapeutics," Associate Professor Papenfuss said. "We hope that in the long term this information will underpin new strategies to prevent and treat scabies infestations, and prevent lifelong complications for people in remote Aboriginal communities."

Computational biology researcher Dr Melissa Davis studies how the behaviour of cells in normal and cancerous tissues is controlled.

INFECTION AND IMMUNITY

Malaria, tuberculosis and HIV are three of the major global infectious diseases causing significant death and disease, particularly in resource-poor countries.

The Infection and Immunity division aims to understand how infectious agents cause human disease and use this knowledge to develop new treatments.

Collaborative centre tackles infections in cancer

Many people with cancer are susceptible to infections because their immune system is weakened, either by the cancer itself, or as a side-effect of anti-cancer treatments.

The new National Health and Medical Research Council Centre for Improving Cancer Outcomes Through Enhanced Infection Services (CRE-IMPACT) is a collaboration between Peter MacCallum Cancer Centre, the Walter and Eliza Hall Institute, Westmead Hospital and the University of Melbourne.

The centre aims to develop strategies that mitigate infections in cancer patients, through early diagnosis and better treatments. Institute researchers, led by Professor Marc Pellegrini, will use genomics and proteomics to predict which patients are at risk of life-threatening infections, and to understand why some patients are at more risk of certain type of infections.

New malaria targets discovered

The invasion of red blood cells is a key step in the malaria parasite's lifecycle within the human body. A research team led by Professor Alan Cowman has discovered a way to stop the malaria parasite invading healthy red blood cells, in a study giving fresh hope to the development of much-needed new antimalarial drug or vaccine.

The team revealed a complex of three proteins that is essential for the ability of the *Plasmodium falciparum* parasite to invade red blood cells. Malaria parasites lacking this complex could not invade red blood cells, halting the progress of the infection.

The team hope that medicines or vaccines that interrupt the protein complex could offer hope as new approaches to malaria prevention or treatment.

Improving treatments for chronic hepatitis B

Two billion people worldwide are infected with hepatitis B virus (HBV) and 240 million people – including more than 200,000 Australians – are chronic carriers of this viral infection. People with chronic HBV infection, which cannot be cured, are at risk of developing liver cirrhosis and liver cancer.

Dr Greg Ebert has received an Australian Centre for HIV and Hepatitis Virology Research Grant to investigate a new, potentially curative approach to treating HBV. Research by Dr Ebert and colleagues has previously shown that a drug called birinapant, which was initially developed as an anti-cancer agent, can treat chronic HBV infection – a study that has now progressed to clinical trials. The grant will enable new research to investigate how birinapant can be combined with other drugs to enhance its antiviral effects.

Health impact

Infectious diseases: chronic infections, dengue fever, hepatitis B, HIV, HTLV-1, malaria, melioidosis, toxoplasmosis, tuberculosis, vaccines

Division heads

Professor Alan Cowman

Professor Marc Pellegrini

Laboratory heads

Dr Justin Boddey

Dr Diana Hansen

Dr Wai-Hong Tham

Associate Professor Chris Tonkin

33 publications

32 staff

30 students

4 clinicians

Dr Wai-Hong Tham (left), Dr Jakub Gruszczyk and colleagues have used structural biology to create a three-dimensional map of a protein that allows the *Plasmodium vivax* malaria parasite to invade red blood cells. This is allowing the team to investigate new targets for a potential malaria vaccine that targets both *P. vivax* and *P. falciparum*, the two species responsible for the majority of malaria infections and deaths worldwide.

Protein map offers new malaria vaccine hope

***Plasmodium vivax* is the predominant form of malaria found outside Africa, imposing a huge burden of disease across South and South East Asia, the Pacific, the Middle East and Central and South America.**

The *P. vivax* parasite hides in a dormant form in the liver, only to re-emerge months later. This makes it the main cause of relapsing malaria infections worldwide and poses challenges for its elimination.

Dr Wai-Hong Tham, Dr Jakub Gruszczyk and colleagues have used structural biology to investigate at the atomic scale how *P. vivax* invades red blood cells.

Understanding how malaria parasites gain entry into red blood cells was essential for developing strategies to prevent malaria, Dr Tham said. "*P. vivax* enters immature red blood cells by making proteins that recognise and bind to receptors on the red blood cell surface.

"THESE TWO SPECIES OF MALARIA ARE RESPONSIBLE FOR THE MAJORITY OF MALARIA INFECTIONS AND DEATHS WORLDWIDE, SO A VACCINE THAT TARGETS BOTH WOULD BE A CRITICAL ADDITION TO OUR ARSENAL"

"We have produced the first three-dimensional, atomic resolution structure of one of these proteins, using the Australian Synchrotron in Melbourne. We now have a map of where the proteins are binding their receptors, which gives us the instructions we need to begin designing inhibitors that could be used in a malaria vaccine."

In another exciting development, the team found the *P. vivax* proteins used to infect red blood cells were structurally almost identical to those used by *Plasmodium falciparum*, the parasite responsible for most malaria deaths.

"The three-dimensional map showed that the proteins in both parasites are folded in the same way," Dr Tham said.

"Now that we have a detailed, atomic resolution map, we are looking for a common part of the protein that could be used to design a vaccine effective in preventing both *P. vivax* and *P. falciparum* malaria. These two species of malaria are responsible for the majority of malaria infections and deaths worldwide, so a vaccine that targets both would be a critical addition to our arsenal."

Dr Tham said there was growing evidence that developing better treatments or preventive strategies for both *P. falciparum* and *P. vivax* malaria was imperative for malaria eradication.

"Experience has shown that effective treatment of *P. falciparum* malaria tends to be accompanied by a resurgence of *P. vivax*, so it is critical to continue looking for better ways to manage both species," she said.

Collaborating divisions

Infection and Immunity, Cell Signalling and Cell Death, Population Health and Immunity

Collaborating organisations

Mahidol University (Thailand), the University of Melbourne

Funding partners

Australian National Health and Medical Research Council, Australian Research Council, Drakensberg Trust, Victorian Government Operational Infrastructure Support Program

More information

Gruszczyk J *et al*. Structurally conserved erythrocyte-binding domain in *Plasmodium* provides a versatile scaffold for alternate receptor engagement. *Proceedings of the National Academy of Sciences USA*.
2016 Jan 12;113(2):E191-200

A step closer to finding a functional HIV cure

Human immunodeficiency virus (HIV) infection places an immense burden on global health. The virus causes acquired immune deficiency syndrome (AIDS) by depleting infection-fighting immune cells. There are medications that are effective in preventing people with HIV developing AIDS, and preventing the spread of the virus, but no cure.

Professor Marc Pellegrini's research is focused on improving treatments for globally significant chronic infections.

The team have discovered that birinapant, a drug originally developed to target and kill cancer cells, may also be effective in selectively killing cells infected with HIV.

"WHAT COULD BE MORE EXCITING THAN THE POSSIBILITY OF GROUNDBREAKING ADVANCES IN MEDICAL HEALTHCARE THAT WILL MAKE A REAL DIFFERENCE TO SO MANY?"

With support from The Phyllis Connor Memorial Trust, managed by Equity Trustees and co-trustee Mr Norman Bourke, Professor Pellegrini and his team have been able to carry out a year of crucial preclinical testing to validate this theory.

The testing has confirmed that anti-cancer drugs such as birinapant show great promise in targetting cells infected with viruses, Professor Pellegrini said. "We now believe this class of drugs has the potential to be harnessed to develop a functional cure for HIV," he said.

"A functional cure does not necessarily mean complete eradication of HIV from the body. Our goal is for the immune system to control HIV on its own, thus preventing further spread of infection.

"A key aim of a functional HIV cure is also to allow patients to discontinue all ongoing therapy, without the virus progressing to AIDS or other HIV-related diseases, such as premature ageing," Professor Pellegrini said.

Ms Helen Rowe, Senior Manager Charitable Trusts at Equity Trustees, said philanthropy could play a vital role in funding medical research such as Professor Pellegrini's, which may use 'outside of the square' thinking.

"Many of the charitable trusts that we manage fund medical research, and nearly half of the $70 million of grants we distribute each year go to health and medical research projects," she said. "What could be more exciting than the possibility of groundbreaking advances in medical healthcare that will make a real difference to so many?

"Equity Trustees is proud to be entrusted with the legacy of so many people who understood the ability of philanthropy to empower change," Ms Rowe said.

Chronic infections persist within our body in the long term, avoiding immune clearance. Professor Marc Pellegrini leads a team investigating how potential new medications could be used to treat chronic infections including hepatitis B and HIV.

IMMUNOLOGY

The Immunology division investigates how immune responses are regulated. Their aim is to improve vaccine performance, treatment of autoimmune and immunodeficient conditions and develop ways to use the immune system to target cancer cells.

Harnessing the immune system to fight brain cancer

Immunotherapy is a new approach to cancer treatment that harnesses the body's own immune system.

Dr Ryan Cross is investigating one type of immunotherapy in which a cancer patient's own immune cells are isolated, genetically modified to become 'super killer cells', and re-infused to fight their cancer. Dr Cross' research is revealing how immunotherapy could be used to treat children with brain cancer. It is hoped that a benefit of immunotherapy over conventional therapies is that it may provide long-lasting protection against cancer recurrence through the persistence of cancer-specific immune memory cells.

This project has been boosted by a two-year grant from The Jack Brockhoff Foundation to Dr Cross.

Equipment funding accelerates flu research

Seasonal influenza causes considerable illness, loss of productivity and death in our community. Current influenza vaccines target viral proteins that change yearly, requiring continuous vaccination generation and distribution.

Dr Joanna Groom is investigating how antiviral T cells fight influenza infections in the lung. Grants from the Rebecca Cooper Foundation and the Harold and Cora Brennen Benevolent Trust, managed by Equity Trustees, have enabled the team to accelerate their research through the acquisition of a new automated cell-separation machine. With the equipment, the team is purifying immune cells from influenza-infected lung tissue to understand how they protect against the virus, with the goal of developing a universal vaccine that provides broad, long-lasting protection against influenza.

Immunology researchers contribute to national society

Researchers in the Immunology division continued their strong support of the Australasian Society of Immunology in 2016.

Professor Andrew Lew's contribution to organising the International Congress in Immunology held in Melbourne led to his receiving life membership of the society and their highest award for service, the Derrick Rowley Medal.

Dr Susanne Heinzel became president of the Australasian Society of Immunology, a role she will hold until late 2018.

Dr Kim Pham and Dr Dimitra Zotos helped coordinate the society's Day of Immunology program, which showcased immunology to the community through public lectures, laboratory tours and a vaccination cafe.

Health impact

Cancers: leukaemia, lymphoma, myeloma

Immune disorders: allergy, coeliac disease, lupus, primary immune deficiencies, transplantation, type 1 diabetes

Infectious diseases: influenza, vaccines

Other areas: personalised medicine

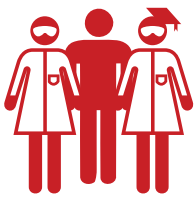
Division head

Professor Phil Hodgkin

Laboratory heads

Dr Daniel Gray
Dr Joanna Groom
Dr Edwin Hawkins
Dr Misty Jenkins
Professor Andrew Lew
Emeritus Professor Jacques Miller
Dr Shalin Naik
Professor Ken Shortman
Dr Jason Tye-Din
Dr Bob Anderson, honorary

40 publications



34 staff
10 students
3 clinicians

Immune cell's destiny inherited from parents

Immune T cells are programmed to recognise different microbes that may cause infection.

When this happens responding T cells are 'activated' and cloned by cell division to create an immune army to fight the infection. The number of immune cells produced and their lifespan is tightly controlled to ensure the infection is successfully eliminated while clearing excess immune cells from the body.

Dr Julia Marchingo, Dr Susanne Heinzel and Professor Phil Hodgkin led a research team that investigated how these two processes – division and clearance – are controlled.

"THIS RESEARCH COULD EXPLAIN SOME OF THE PROBLEMS THAT CONTRIBUTE TO AUTOIMMUNE DISORDERS"

Working with collaborators at the National University of Ireland, Maynooth, the team developed new techniques to trace single cells, including computational biology approaches to follow the behaviour of hundreds of individual cells.

The team revealed that different 'families' of T cells varied in how many times the cells would divide, and at what point during the immune response they died, said Dr Marchingo. "However we were surprised by how consistent this timing was within each family of cells – as if related cells had inherited a set of instructions specifying how they should behave."

Dr Heinzel said they discovered T cells had a given amount of time in which they could divide. "Irrespective of how many divisions have actually occurred, once the time has run out, no more divisions can happen," she said.

A protein called Myc acted as the cell division clock, Dr Heinzel said. "At the start of an immune response, responding T cells are allocated a certain amount of Myc," she said. "This diminishes over time and, once the cell runs out of Myc, the time is up and division stops. The more Myc there is, the more time the cells have to divide."

Professor Hodgkin said the team's discovery was an important advance in understanding how immune responses are controlled. "As well as providing new insights into how we protect ourselves from infection, this research could explain some of the problems that contribute to autoimmune disorders, when the immune system mistakenly attacks the body, as well as underpinning advances in vaccination technology," he said.

Collaborating divisions

Immunology, Molecular Immunology

Collaborating organisations

National University of Ireland, Maynooth, University of Melbourne

Funding partners

Australian National Health and Medical Research Council, Australian Postgraduate Awards, Cancer Council Victoria, the European Union Seventh Framework Programme, Alan Harris Scholarship Fund, Melbourne International Research and International Fee Remission Scholarships, Edith Moffat Scholarship, Science Foundation Ireland, Victorian Government Operational Infrastructure Support Program

More information

Marchingo JM *et al*. T-cell stimuli independently sum to regulate an inherited clonal division fate. ***Nature Communications*****. 2016 Nov 21;7:13540**

Heinzel S *et al*. A Myc-dependent division timer complements a cell-death timer to regulate T cell and B cell responses. ***Nature Immunology*****. 2017 Jan;18(1):96-103**

Immunotherapy is a promising new approach to treating cancer, by unleashing the immune system against cancer cells.

A grant from The Jack Brockhoff Foundation is enabling Dr Ryan Cross to investigate how immunotherapy could be used to treat children with brain cancer.

Examining the gluten-free diet: why does it fail?

Coeliac disease is an autoimmune condition affecting one in 70 Australians. It is caused by an immune reaction to gluten, a food protein found in wheat, rye, barley and oats.

Untreated coeliac disease causes digestive symptoms such as bloating, abdominal pain and diarrhoea, and can lead to anaemia, low iron levels and excessive tiredness. It also increases the risk of serious illnesses such as other autoimmune diseases, osteoporosis and some cancers.

> "WE WANT TO DISCOVER WHY THE GLUTEN-FREE DIET FAILS"

Adherence to a gluten-free diet is the only way to treat coeliac disease, yet half of all Australian adults with coeliac disease still experience disease symptoms or intestinal damage despite many years of avoiding gluten-containing foods.

Two grants from Coeliac Australia are allowing the Institute's coeliac disease research team, led by scientist and gastroenterologist Dr Jason Tye-Din, to scrutinise the diets of Australians with coeliac disease.

Specialist dietitian Dr Emma Halmos will use the funding to investigate the reasons why the gluten-free diet doesn't always work as intended. She said the findings would be critical to improving the treatment all coeliacs depend on.

"The cause of ongoing intestinal inflammation or symptoms in people with coeliac disease is often attributed to accidental or low amounts of gluten exposure but why this happens and what causes it is poorly understood," Dr Halmos said.

"We want to discover why the gluten-free diet fails. We will explore whether it is because of problems in the testing and labelling of food as gluten-free when it actually contains gluten, contamination of gluten-free foods during food preparation and sale, or difficulties people with coeliac disease may have with understanding and complying with a strict gluten-free diet."

A second study led by Dr Melinda Hardy is determining whether oats are a safe food for people with coeliac disease. "Oats are a highly nutritious cereal but Australian coeliac patients are instructed to exclude them from their diet as they are potentially harmful," Dr Hardy said. "We will investigate why some coeliacs get sick when eating oats, determine if a dose or type of oats can be safely consumed, and develop a food test to identify the unsafe parts of oats."

Funding from Coeliac Australia is allowing coeliac disease researchers Dr Jason Tye-Din (left), Dr Emma Halmos (centre) and Dr Melinda Hardy (right) to scrutinise the diets of Australians with coeliac disease, to understand factors that may make the gluten-free diet fail.

CELL SIGNALLING AND CELL DEATH

The Cell Signalling and Cell Death division investigates the molecular mechanisms by which cells kill themselves, and the control processes that switch cell death on and off.

Many diseases are characterised by too much or too little cell death. Understanding how cell death processes are controlled will help us to develop new treatments for cancers and immune disorders.

New clues to how necroptotic cell death evolved

The protein MLKL is essential for triggering necroptosis, a recently defined form of cell death that triggers inflammation. In healthy cells MLKL is switched off, but responds to stimuli – such as certain viral infections – to activate and kill the infected cell.

PhD student Ms Maria Tanzer and Dr James Murphy compared versions of the MLKL protein from diverse vertebrate species to determine whether necroptosis has been conserved during evolution. Their research revealed that although the MLKL from all species studied contained the components that trigger necroptotic cell death, there was considerable variation between species in how MLKL was activated. This suggests that although necroptosis controlled by MLKL has been conserved during vertebrate evolution, the control of MLKL differs between species.

Inflammatory cytokine release separated from cell death

The cytokine interleukin-1β is a potent trigger of inflammation. It is critical for providing immunity to invading microorganisms, but – if excessively or inappropriately produced – can also trigger inflammatory diseases.

Interleukin-1β is produced as a longer, inactive form that becomes activated when it is cut by an enzyme called caspase-1. Because caspase-1 can also trigger cell death, a controversial question in the field has been whether active interleukin-1β is only secreted by dying cells.

Ms Stephanie Conos, Dr Lisa Lindqvist and Dr James Vince have investigated this question by generating systems that enabled the analysis of interleukin-1β cleavage by caspase-1 in living cells. This study revealed that interleukin-1β secretion can occur from living cells. Further insights into this process may reveal new targets for the treatment of inflammatory diseases driven by interleukin-1β.

Necroptosis relies on 'chaperone' protein

Necroptotic cell death has been implicated in the development of a range of inflammatory, autoimmune and neurodegenerative diseases. Ms Annette Jacobsen, Associate Professor Guillaume Lessene and Dr James Murphy are looking at how necroptosis might be prevented by potential new therapeutics, as a way of treating these diseases.

Their work has focused on inhibiting the protein MLKL, which directly causes necroptotic cell death. The team screened a library of drug-like compounds and identified that they could stop necroptosis by inhibiting a protein called HSP90, a 'chaperone' protein that helps other cellular proteins to fold correctly. The team showed HSP90 was essential for MLKL-controlled necroptosis, and could be a potential drug target for treating disease by preventing necroptosis.

Health impact

Cancers: bowel cancer, breast cancer, leukaemia, lung cancer, lymphoma, myeloproliferative disorders, stomach cancer

Immune disorders: inflammatory bowel disease, psoriasis, rheumatoid arthritis

Division heads

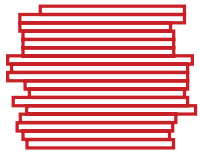
Professor John Silke

Professor David Vaux

Laboratory heads

Dr Grant Dewson

Dr James Murphy



43 publications

23 staff

15 students

1 clinician

Inflammation is critical for providing immunity to infections, but excessive inflammation can also drive inflammatory diseases.

Dr Lisa Lindqvist and colleagues are investigating how a potent trigger of inflammation, interleukin-1β, is secreted from cells.

New drug combinations show promise for acute myeloid leukaemia

Acute myeloid leukaemia (AML) causes around 850 deaths in Australia each year, more than any other type of blood cancer. Many people with AML respond poorly to treatment, with fewer than one-third surviving for five years after their diagnosis.

Two studies led by Professor John Silke have shown that combinations of recently developed anti-cancer agents may be effective new treatments for AML.

Dr Najoua Lalaoui and colleagues demonstrated that the combination of two agents, birinapant and p38 inhibitors, was more effective in treating AML in preclinical models than either agent alone.

The current treatment for people with AML, high-dose chemotherapy, has many toxic side-effects, Dr Lalaoui said. "Both p38 inhibitors and birinapant have been safely used in clinical trials," she said. "We are hopeful that combining the agents may be a more effective, less toxic treatment for people with AML than current therapies."

"The drug combination could even kill forms of AML that are highly resistant to chemotherapy, which is great news," Dr Lalaoui said.

In a second study, Dr Gabriela Brumatti, PhD student Ms Chunyan Ma and Professor Paul Ekert from the Murdoch Children's Research Institute showed that a combination of birinapant and emricasan, a US Food and Drug Administration-approved drug, could also kill AML in preclinical models.

Dr Brumatti said emricasan works by switching off 'apoptotic' cell death, unleashing an alternate form of cell death called necroptosis. "It had been speculated that inducing necroptosis might be an effective way to kill cancer cells", she said. "We discovered this was the case, suggesting birinapant and emricasan could be a clinically feasible and safe approach to treating AML.

"This approach is an exciting new development, as cancer cells often acquire resistance to apoptosis. We hope this drug combination could be effective against otherwise impossible-to-treat leukaemias," Dr Brumatti said.

Professor Silke said these discoveries were underpinned by two decades of research at the Institute into the inhibitors of apoptosis proteins that are targeted by birinapant.

"Birinapant has been used in clinical trials for several types of cancers," Professor Silke said. "Our latest research is part of an exciting next step, enhancing the anti-cancer effects of birinapant."

Birinapant was developed by TetraLogic Pharmaceuticals Corporation based in Malvern, US, and is being clinically evaluated by Swedish oncology company Medivir AB.

Collaborating divisions

Cell Signalling and Cell Death, Cancer and Haematology, Systems Biology and Personalised Medicine

Collaborating organisations

The Alfred Hospital, Burnet Institute, Children's Cancer Institute, Murdoch Children's Research Institute, Monash University, Peter MacCallum Cancer Centre, Sanford-Burnham Medical Research Institute (US), TetraLogic Pharmaceuticals Corporation (US), University of New South Wales, University of Zurich (Switzerland)

Funding partners

Association pour le Recherche contre le Cancer (France), Australian Cancer Research Foundation, Australian National Health and Medical Research Council, Cancer Council Victoria, German Research Foundation, Leukemia & Lymphoma Society (US), Peter Müller Fellowship (Switzerland), Victorian Government Operational Infrastructure Support Program

More information

Brumatti G *et al*. The caspase-8 inhibitor emricasan combines with the SMAC mimetic birinapant to induce necroptosis and treat acute myeloid leukemia. *Science Translational Medicine*. 2016 May 18;8(339):339ra69

Lalaoui N *et al*. Targeting p38 or MK2 enhances the anti-leukemic activity of Smac-mimetics. *Cancer Cell*. 2016 Sep 12;30(3):499-500

Improving treatments for triple-negative breast cancers

Breast cancers can be divided into different subtypes based on the presence or absence of three cell surface hormone receptors called the oestrogen receptor, the progesterone receptor and Her2/Neu. These receptors, which can be targeted by 'hormone therapies', influence the choice of treatment for people with breast cancer.

So-called triple-negative breast cancers, making up 15 to 20 per cent of all breast cancers, lack all three receptors. These cancers do not respond to hormone therapies, and the only current treatment is conventional chemotherapy. People diagnosed with triple-negative breast cancers have a greater risk of recurrence and death than people with hormone-receptor expressing breast cancer.

"WE WERE EXCITED TO SEE THAT TRIPLE-NEGATIVE BREAST CANCERS WERE SENSITIVE TO BIRINAPANT, BECAUSE THIS COULD BE A NEW WAY TO TREAT THESE CANCERS"

Dr Najoua Lalaoui, Professor John Silke and Professor David Vaux have investigated a potential new approach to treating triple-negative breast cancer.

By studying breast cancer cells growing in the laboratory, the researchers discovered that a potential anti-cancer agent called birinapant was particularly effective in killing triple-negative breast cancers, Dr Lalaoui said.

"Birinapant is a new type of drug called a SMAC-mimetic, which kills cells by targetting the cell death machinery," Dr Lalaoui said. "We were excited to see that triple-negative breast cancers were sensitive to birinapant, because this could be a new way to treat these cancers."

A three-year grant from Worldwide Cancer Research has enabled Dr Lalaoui and Professor Vaux to collaborate with the Institute's breast cancer laboratory, led by Professor Geoff Lindeman and Professor Jane Visvader, to continue this work.

"We are investigating whether birinapant could be combined with existing therapies to effectively treat triple-negative breast cancers," she said. "We hope to identify a combination therapy that will improve the outcomes for people with triple-negative breast cancers.

"We also hope to develop better ways to predict which breast cancers respond to birinapant. This would allow treatment for a patient to be personalised, so that every person with breast cancer gets the best treatment for their disease," Dr Lalaoui said.

Professor John Silke (centre) and Dr Najoua Lalaoui (right) are investigating new combination therapies for cancer.

Their research team has worked closely with Pam, a community representative, through the Institute's consumer-researcher buddy system.

INFLAMMATION

The Inflammation division seeks to understand the complex series of biological and molecular events that regulate inflammation.

Our aim is to improve the diagnosis, treatment and prevention of human inflammatory diseases such as rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, rheumatic fever and inflammation that leads to cancer.

Clinical trials of new G-CSF antibody

A discovery by Institute researchers about how inflammation is triggered has underpinned clinical trials of a potential new treatment for inflammatory and autoimmune diseases.

Preclinical research led by Professor Ian Wicks, who is also head of Rheumatology at The Royal Melbourne Hospital, identified the cell signalling factor G-CSF as a critical driver of inflammation in rheumatoid arthritis, an autoimmune disease that damages the joints and other tissues.

CSL324 is a human monoclonal antibody that neutralises G-CSF. It was developed by Australian biopharmaceutical company CSL, through a collaboration with the Institute and MuriGen, a drug discovery company established by the Institute. Phase 1 clinical trials of CSL324 commenced in 2016.

New drugs may combat fatal bacteria

Legionnaires' disease is a potentially fatal lung infection caused by *Legionella* bacteria. These bacteria can hide within human cells called macrophages, escaping the body's immune defences and being shielded from many types of antibiotics.

Dr James Vince and colleagues at the Monash University Biomedicine Discovery Institute discovered that a cell survival protein called BCL-XL is an Achilles' heel of *Legionella*-infected macrophages. Turning off BCL-XL with compounds known as BH3-mimetics killed the infected cells — but not uninfected cells — allowing the infection to be cleared from the body.

This study was the first to show BH3-mimetics can successfully treat bacterial infections, and may offer a new approach to treating other intracellular bacteria, including antibiotic-resistant strains.

Targetting pancreatic cancer growth signals

Dr Tracy Putoczki leads a team investigating how a signalling molecule called interleukin-11 promotes pancreatic cancer. Tumours receive and respond to signals such as interleukin-11 that are produced by the surrounding non-cancerous tissue, which support the cancer's growth, metastasis and resistance to chemotherapy.

To further advance this research, Dr Putoczki's team recently received a four-year, $920,000 grant from the Australian National Health and Medical Research Council to pinpoint the exact cells in the pancreas that produce interleukin-11, and the cells within the tumour that respond to interleukin-11. The project aims to define the 'conversation' between tumour cells and their environment, and to understand how inhibiting interleukin-11 might offer a novel approach to treating pancreatic cancer in the future.

Health impact

Cancers: bowel cancer, myeloproliferative disorders, pancreatic cancer, stomach cancer

Immune disorders: inflammatory bowel disease, lupus, psoriasis, rheumatic fever and heart disease, rheumatoid arthritis

Infectious diseases: chronic infections, influenza, legionnaires' disease

Division head

Professor Ian Wicks

Laboratory heads

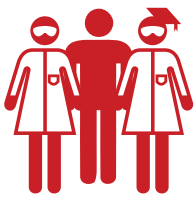
Dr Seth Masters

Dr Sandra Nicholson

Dr Tracy Putoczki

Dr James Vince

35 publications



36 staff

11 students

7 clinicians

Trigger identified for inflammatory heart disease

Kawasaki disease is a serious condition, predominantly affecting young children, in which blood vessels become inflamed.

In around a quarter of patients the inflammation involves the blood vessels within the heart, causing immediate or longer-term damage. As a result, Kawasaki disease is a leading cause of paediatric heart disease in developed countries, including Australia.

"WE WERE EXCITED TO DISCOVER THAT BLOCKING GM-CSF FUNCTION EARLY IN THE DISEASE OFFERED NEAR-COMPLETE PROTECTION AGAINST CARDIAC INFLAMMATION"

It is not known what causes Kawasaki disease, although a combination of infectious triggers and genetic susceptibility are suspected. Institute researchers Dr Angus Stock and Professor Ian Wicks, and colleagues at industry partners CSL and MedImmune, have led a new study into how heart inflammation occurs in a laboratory model of Kawasaki disease.

Professor Wicks, who is also head of Rheumatology at The Royal Melbourne Hospital, said cardiac inflammation in Kawasaki disease was associated with the infiltration of immune cells into the heart.

"Our study investigated what signals were bringing these cells into the heart," he said. "We hypothesised that blocking these signals might be a way to reduce the inflammation and subsequent heart damage that occur in Kawasaki disease."

The team discovered that a cell-signalling hormone called GM-CSF – one of the 'colony stimulating factors' or CSFs discovered at the Institute in the 1970s – was an essential driver of heart inflammation.

Dr Stock said this was the first time GM-CSF had been pinpointed as a player in Kawasaki disease. "We were able to show that early in the disease, heart tissue releases GM-CSF," he said. "This drives a series of events that attract immune cells into the heart and promote the damaging inflammation.

"We were excited to discover that blocking GM-CSF function early in the disease offered near-complete protection against cardiac inflammation. This is an important finding as it suggests that when Kawasaki disease is diagnosed, blocking GM-CSF could be a way to prevent the serious cardiac complications that can occur," Dr Stock said.

Professor Wicks said that the Institute had a longstanding collaboration with CSL and MedImmune on the development of new therapeutic antibodies that inhibit GM-CSF. "We are now broadening our studies, including investigating clinical cases of Kawasaki disease, to determine whether blocking GM-CSF should be considered as a new therapeutic approach for children with Kawasaki disease," he said.

Collaborating organisations

CSL, MedImmune, The Royal Children's Hospital, The Royal Melbourne Hospital

Funding partners

Australian National Health and Medical Research Council, CSL, MedImmune, National Heart Foundation, John T Reid Charitable Trusts, Victorian Government Operational Infrastructure Support Program

More information

Stock AT *et al.* GM-CSF primes cardiac inflammation in a mouse model of Kawasaki disease. *The Journal of Experimental Medicine.* 2016 Sep 19;213(10):1983-98

Communication between cells is vital for the coordinated functioning of our body. Recently the molecule RNA has been identified as a messenger that can be transferred from one cell to another, although the significance of this type of cell-to-cell communication in the body is currently unclear.

PhD student Ms Marilou Barrios is investigating the types of messages that might be transmitted by RNA signalling in the body.

Community funding supports rare disease research

People with periodic fever syndromes experience frequent and debilitating episodes of inflammatory symptoms, including fevers, that are not associated with an infectious cause.

Mrs Melissa Bowyer's young son Riley has a rare periodic fever syndrome, called PFAPA, that causes high fevers, swollen neck glands and body pain every two to three weeks. There is currently no effective treatment for PFAPA.

Mrs Bowyer said it was not known whether Riley would eventually outgrow the disease. "As this illness is so rare, it does not attract a lot of funding and research," Mrs Boyer said.

"IT IS INSPIRING TO HAVE THE INVOLVEMENT OF THE COMMUNITY IN OUR RESEARCH"

Mrs Bowyer is raising money for research into periodic fever syndromes, which she hopes will improve the understanding of these diseases and potentially lead to improved approaches to diagnosis and treatment. In 2016 she took part in the Blackmores Sydney Running Festival and has so far raised more than $7900.

This funding is supporting Dr Seth Masters' research into periodic fever syndromes, which is investigating the molecules that trigger the disease-causing inflammation.

In 2016 Dr Masters led an international research study that identified a new periodic fever syndrome that they named 'pyrin associated auto-inflammation with neutrophilic dermatosis' (PAAND). This disease is caused by defects in a protein called pyrin, which normally triggers inflammation in response to infections, but in PAAND it spontaneously triggers unnecessary inflammation. Importantly, by defining the cause of PAAND, the researchers found a new therapeutic approach that targeted the underlying molecules, which has so far resulted in dramatic disease resolution in all patients treated.

Dr Masters said he hoped his future research might shed light on what causes PFAPA as well. "Our team has spent many years unravelling the molecules that drive inflammation," Dr Masters said. "We are now at the stage of being able to apply that knowledge to help people with periodic fever syndromes and other auto-inflammatory diseases, which is a really important outcome."

The Bowyer family recently came to the Institute to meet Dr Masters and learn about his research.

"It is inspiring to have the involvement of the community in our research," Dr Masters said.

Community fundraiser Mrs Melissa Bowyer (centre back) and her family visited Dr Seth Masters (left) to learn about his research into periodic fever syndromes.

Mrs Bowyer has raised more than $7900 for this research, which she hopes will improve the understanding of these diseases and potentially lead to improvements in their diagnosis and treatment.

MOLECULAR IMMUNOLOGY

The Molecular Immunology division aims to understand how the immune system functions to protect us from pathogens, such as bacteria and viruses, but ignores the harmless or beneficial microbes in our environment.

By understanding the normal immune response, we aim to pinpoint the events that go awry in diseases such as lymphoma, autoimmunity and chronic infections.

Earliest immune ancestor revealed

The innate immune system is the first line of defence against invading microorganisms, and mediates tissue repair and inflammation.

Dr Cyril Seillet and colleagues investigated the development of innate lymphoid cells, a family of cells that enable protective immunity, identifying the earliest 'ancestor' (progenitor) of all innate lymphoid cells.

While cataloguing the surface proteins of these early progenitors, they identified the molecule PD-1 – a target for existing cancer immunotherapy drugs. The team will now determine how these surface proteins might be modified to dampen inflammation as a way of treating inflammatory diseases, or to enhance anti-cancer immune responses.

Gene implicated in long-term antibody production

Antibody production is an essential arm of the immune response. Antibodies provide immediate protection against infection, and the persistence of antibody-producing cells for years or decades in the body is vital for long-term immunity.

Dr Julie Tellier and colleagues study the long-lived antibody-producing cells that develop from B cells following infection or vaccination. They investigated the role of the gene *Blimp-1*, which is essential for the formation of antibody-producing cells, but whose role in the function of the mature long-lived cells was poorly understood.

Deleting *Blimp-1* from mature antibody-producing cells rendered the cells incapable of secreting protective antibodies, demonstrating *Blimp-1* is essential for antibody secretion, which underpins long-term protective immunity.

The changing fates of killer T cells

Viruses and some bacteria hide within the cells of our body. Our immune system employs different types of killer T cells to fight these infections and generate long-term immunity. 'Effector' killer T cells actively destroy infected cells, while 'memory' killer T cells lie dormant, only reawakening if the infection returns.

Dr Dane Newman, Dr Rhys Allan and colleagues identified that the protein KAT6A controlled the fate of killer T cells by changing the DNA structure to 'fine-tune' the level of cell surface receptors. Understanding the processes that produce both effector and memory killer T cells could help to improve vaccine design and cancer immunotherapies.

Health impact

Cancers: leukaemia, lymphoma, melanoma, myeloma

Immune disorders: allergy, asthma, inflammatory bowel disease, lupus, multiple sclerosis, type 2 diabetes

Infectious diseases: influenza, listeria, vaccines

Division head

Professor Stephen Nutt

Laboratory heads

Dr Rhys Allan
Professor Gabrielle Belz
Professor Lynn Corcoran
Dr Joanna Groom
Dr Nicholas Huntington
Dr Axel Kallies
Professor Li Wu, honorary

59 publications

39 staff
14 students
3 clinicians

Innate immune cells are critical frontline defenders of our body, providing a rapid inflammatory response to microbial invasions. However prolonged inflammation may also contribute to the development of certain cancers.

Support from Cure Cancer Australia has enabled Dr Lisa Mielke to investigate whether innate immune cells contribute to bowel cancer.

Keeping 'local heroes' at immune frontline

Our bodies are constantly exposed to disease-causing microbes, most of which are eliminated by our immune system. Immune 'memory' cells play a crucial role in this process, providing long-term immune protection against future exposure to the same microbes.

A specialised type of T cell, called tissue-resident memory T cells, stand guard at the 'front lines' where microbes often attempt to gain entry to the body – such as the skin and gut. These cells are particularly important because they immediately act to prevent infection before it can take hold and spread.

Dr Axel Kallies, Dr Klaas van Gisbergen and Dr Wei Shi, with collaborators including Dr Laura Mackay from the Peter Doherty Institute for Infection and Immunity at the University of Melbourne, uncovered the genes that keep tissue-resident memory T cells in organs such as the skin and gut.

"UNDERSTANDING HOW IMMUNE CELLS REMAIN AT THESE CRITICAL SITES IS ESSENTIAL IN DEVELOPING BETTER WAYS TO PROTECT US FROM INFECTIONS"

The team showed that two genes, *Hobit* and *Blimp1*, control a universal molecular program responsible for placing these cells at the front lines to fight infection.

Dr Kallies said the presence of these tissue-resident memory T cells, which differ strikingly from their counterparts circulating in the blood stream, was key to local protection against viruses and bacteria.

"Understanding how immune cells remain at these critical sites is essential in developing better ways to protect us from infections," Dr Kallies said.

"Discovering these 'local heroes' and knowing how they develop and how they are maintained allows us to find ways to ensure memory T cells are positioned where they are needed most."

The findings may also help improve the effectiveness of vaccines.

"When immune memory is induced by a vaccine, we want to ensure the memory T cells localise to the front lines for maximum protection. Our research has shown *Hobit* and *Blimp-1* are key for this strategy," Dr Kallies said.

"This research will help us understand how tissue-resident memory T cells adapt, survive and respond within the organs they protect. This is critical to rid the body of pathogens even before they are established and may also have implications for understanding how the spread of cancer could be prevented."

Collaborating divisions

Molecular Immunology, Bioinformatics, Infection and Immunity

Collaborating organisations

Peter Doherty Institute for Infection and Immunity, the University of Amsterdam (Netherlands), the University of Melbourne, Vienna Biocenter (Austria)

Funding partners

Alexander von Humboldt Foundation (Germany), Australian National Health and Medical Research Council, Boehringer Ingelheim (Germany), European Community's Seventh Framework Programme, German Research Foundation, Landsteiner Foundation of Blood Transfusion Research (Netherlands), Netherlands Organization of Scientific Research, Victorian Government Operational Infrastructure Support Program, The Viertel Charitable Foundation

More information

Mackay LK *et al*. Hobit and Blimp1 instruct a universal transcriptional program of tissue residency in lymphocytes. *Science*. 2016 Apr 22;352(6284):459-63

Harnessing the immune system to treat advanced melanoma

Melanoma is the most serious form of skin cancer, accounting for around 10 per cent of all new cancers diagnosed in Australia each year.

If melanoma has spread – or metastasised – from its original site before it can be treated, the outlook for patients is particularly poor.

Dr Nick Huntington and his team are investigating how our immune response could be harnessed to fight cancers such as melanoma – an approach known as immunotherapy.

"WE SEE A NEED TO DEVELOP A MORE DIVERSE RANGE OF IMMUNOTHERAPIES – INCLUDING THERAPIES USING NK CELLS – TO EFFECTIVELY TREAT, AND PERHAPS EVEN CURE, METASTATIC MELANOMA"

The team focuses on a type of immune cell called natural killer (NK) cells, which identify and kill abnormal cells in the body, including cancers. In more than a decade working on NK cells, Dr Huntington has identified important processes controlling these cells' development and function.

Several new immunotherapies have been approved recently as treatments for metastatic melanoma, Dr Huntington said.

"However these therapies have focused on enhancing the anti-melanoma response of another type of immune cell, called T cells. We see a need to develop a more diverse range of immunotherapies – including therapies using NK cells – to effectively treat, and perhaps even cure, metastatic melanoma," Dr Huntington said.

A three-year research grant from the Harry J. Lloyd Charitable Trust is enabling Dr Huntington's team to pursue new strategies to boost NK cells' ability to attack melanoma cells.

One aspect of this work is to understand how cell-signalling hormones in and around a melanoma tumour can impact NK cell function.

"In 2016 we made significant discoveries about how NK cell function is controlled by external signals, and to understand how these were transmitted into the cells," Dr Huntington said.

"We hope that this will help us to develop new therapeutic approaches to enhance NK cell function, which we believe will improve the body's ability to fight melanoma."

Immunotherapy is a promising new approach to treating cancer, which harnesses the immune system to attack cancer cells. Dr Nick Huntington leads a team that is investigating the function of natural killer cells, an important arm of the anti-cancer immune response.

SYSTEMS BIOLOGY AND PERSONALISED MEDICINE

The Systems Biology and Personalised Medicine division uses high-throughput technologies to understand global changes in biological systems, and to inform therapeutic decisions. The technologies – including genomics, transcriptomics, proteomics, chemical and genetic screens – are improving our understanding of cancers, immune disorders and infectious diseases.

New discoveries through dynamic imaging

The combination of advanced imaging technologies and powerful computational resources is allowing medical researchers to visualise biological mechanisms and behaviours, to gain insights into how diseases develop, spread and respond to treatment.

The *2016-2020 Centre for Dynamic Imaging Strategic Plan* will guide investment in infrastructure, technology and people to position the centre as a world leader in imaging.

A focus for the centre will be to push existing technologies to the limits and implement cutting-edge, open source platforms. The strategic plan emphasises the importance of ensuring that the application and adaptation of imaging technologies are driven by the needs of scientific research and that technologies are highly adaptable to scientific problems.

Predicting rectal cancer recurrence

Cancers of the rectum, the part of the bowel closest to the anus, are usually treated by chemotherapy and radiotherapy followed by surgery. Predicting the minority of patients whose tumours will recur – and who should therefore receive ongoing treatment – has been a challenge for oncologists.

Associate Professor Peter Gibbs, Associate Professor Jeanne Tie and colleagues have developed a blood test that detects fragments of tumour DNA to indicate which rectal cancer patients are at high risk of recurrence. A project grant from the Australian National Health and Medical Research Council is enabling the team to determine whether selecting treatments for rectal patients according to their blood test results is an efficient and effective strategy.

New gene editing libraries deployed

A grant from the Australian Cancer Research Foundation (ACRF) enabled the opening of the ACRF Breakthrough Technologies Laboratory in 2015. Researchers at the Institute and partner organisations in the Victorian Comprehensive Cancer Centre are using the facility to gain new insights into how cancer develops and how it can be more effectively treated.

A centrepiece of the laboratory is an Australian-first system that uses CRISPR technology to modify specific genes in cancer cells. In 2016 new libraries of 80,000 molecules were deployed that allow researchers to rapidly and precisely alter any single gene within a cancer cell's genome. These are being used to discover genes that are crucial drivers of cancer development, progression and resistance to anti-cancer treatments.

Health impact

Cancers: bowel cancer, leukaemia, lymphoma, melanoma, pancreatic cancer, rectal cancer, stomach cancer

Immune disorders: rheumatoid arthritis, rheumatic fever and heart disease

Infectious diseases: malaria, vaccines

Other areas: antivenoms, congenital disease, personalised medicine

Division head

Professor Liam O'Connor

Laboratory heads

Associate Professor Peter Gibbs
Mr Simon Monard
Dr Kelly Rogers
Dr Hélène Jousset Sabroux
Associate Professor Oliver Sieber
Associate Professor Ian Street
Dr Andrew Webb
Dr Stephen Wilcox

41 publications

77 staff
7 students
9 clinicians

An end to unnecessary chemotherapy

If bowel cancer is detected early, surgical removal alone is often a highly effective treatment for most people.

Scientists have developed a new blood screening test that determines a patient's risk of bowel cancer recurring after surgery, ending the unnecessary use of chemotherapy in patients who are unlikely to experience a relapse.

Researcher Associate Professor Jeanne Tie, who is also a medical oncologist at the Western Hospital and the Peter MacCallum Cancer Centre, said surgery alone was able to cure the majority of cases of stage 2 bowel cancers.

"WITH THIS SIMPLE BLOOD TEST, WE CAN IDENTIFY WHICH PATIENTS ARE LIKELY TO EXPERIENCE A RELAPSE OF BOWEL CANCER."

"Unfortunately, until now we couldn't identify which patients were at risk of cancer recurrence after surgery," Associate Professor Tie said. "Because current methods of predicting recurrence are imprecise, doctors have erred on the side of caution and given chemotherapy to all people with stage 2 bowel cancer following surgery."

Stage 2 bowel cancers occur when the tumour has invaded the bowel wall but not spread to other organs. Up to 40 per cent of patients with stage 2 bowel cancers undergo chemotherapy, even though only a small fraction are likely to experience a cancer relapse.

Clinician-scientists Associate Professor Tie and Associate Professor Peter Gibbs, with international partners from Ludwig Cancer Research and the Johns Hopkins Kimmel Cancer Center, US, developed the blood test, which detects fragments of DNA shed from bowel cancer cells. By following 230 people with stage 2 bowel cancers in 13 Australian hospitals over four years, the team were able to correlate the profile of cancer cell DNA in their blood with their clinical outcomes.

"With this simple blood test, we can identify which patients are likely to experience a relapse of bowel cancer," Associate Professor Tie said. "In the future this means we can better target post-operative chemotherapy to those people who actually need it, and spare those patients who will not benefit from this additional treatment."

Associate Professor Tie's research was described as one of the year's top clinical cancer advances by the American Society of Clinical Oncology.

Collaborating organisations

The Alfred Hospital, Eastern Health, Johns Hopkins Kimmel Cancer Center (US), Ludwig Institute for Cancer Research (US), Monash University, Peter MacCallum Cancer Centre, Queen Elizabeth Hospital, The Royal Melbourne Hospital, the University of Melbourne, Warrnambool Hospital, Western Health

Funding partners

Australian National Health and Medical Research Council, the Conrad N. Hilton Foundation, Sol Goldman Sequencing Facility at Johns Hopkins (US), Ludwig Cancer Research (US), National Institutes of Health, Victorian Cancer Agency, Victorian Government Operational Infrastructure Support Program

More information

Tie J *et al.* Circulating tumor DNA analysis detects minimal residual disease and predicts recurrence in patients with stage II colon cancer. *Science Translational Medicine.* 2016 Jul 6;8(346):346ra92

Until now, clinicians had no reliable way to predict which bowel cancer patients are at risk of cancer recurrence after surgical treatment.

Associate Professor Jeanne Tie and collaborators have developed a new blood test that identifies which patients are at risk of cancer recurrence, allowing these people to receive post-operative chemotherapy.

Gift sheds light on drug-resistant bowel cancers

The past 50 years of medical research has led to many advances in cancer therapy.

Better approaches to diagnosis and treatment have improved the rates of survival for most cancer types. Unfortunately there are still many people with cancer who respond poorly to available treatments, or whose cancers develops resistance to treatment.

A gift from the Janko-Inge Foundation is enabling a research team led by Professor Liam O'Connor to investigate why some people's cancers become resistant to chemotherapy.

> "IN THE FUTURE I AM CERTAIN THAT WE WILL SEE A SHIFT IN CANCER TREATMENT"

Resistance to a therapy is generally a result of genetic changes within the cancer cells, Professor O'Connor said.

"Until now, the way that cancer has been treated can be considered a 'one size fits all' approach," he said. "We still consider cancers in broad categories, and select the treatment based on what is most likely to work.

"In some people, a treatment will be effective for a period of time, killing most of the cancer cells, but a few rogue cells will develop resistance and re-grow. By the time doctors realise that one approach isn't working, valuable time has been lost and the cancer has progressed," Professor O'Connor said.

Chemotherapy resistance is a significant challenge for some types of cancer, such as bowel cancer, with more than 15,000 Australians diagnosed each year.

"We are investigating whether we can identify the genetic changes that lead to chemotherapy resistance in bowel cancer," Professor O'Connor said.

"If we can develop a quick way to identify how effective a particular type of chemotherapy will be for a bowel cancer patient, they can be matched with the best treatment for their disease."

The research may also indicate new approaches to treating bowel cancer, and may be applicable to other types of cancer.

"By pinpointing the genetic changes that cause chemoresistance, we may reveal potential new molecular targets for treating that disease – hopefully leading to new anti-cancer agents, or new combinations of existing agents," Professor O'Connor said.

"In the future I am certain that we will see a shift in cancer treatment – and a consequent improvement in outcomes for people with cancer – by moving towards more personalised strategies where gene sequencing data is used to determine the most effective treatment for an individual with cancer."

A gift from the Janko-Inge Foundation is supporting Professor Liam O'Connor's team to investigate why some cancers become resistant to chemotherapy.

Their research may also lead to a better approach to matching cancer patients to the best type of chemotherapy for their disease.

DEVELOPMENT AND CANCER

The Development and Cancer division investigates cell growth and differentiation in normal embryonic development and in cancer. Molecular mechanisms that enable the rapid, yet regulated, growth of cells during embryonic development are frequently disrupted in cancer. Our researchers aim to identify potential new targets for cancer therapies by better understanding these mechanisms.

Survival factor identified in developing blood vessels

The formation of new blood vessels, called angiogenesis, matches the size of blood vessel networks to the metabolic needs of the surrounding tissues. Angiogenesis is critical during development and growth, but also contributes to diseases such as cancer and the eye diseases diabetic retinopathy and wet age-related macular degeneration.

Ms Emma Watson, Dr Leigh Coultas and colleagues investigated the factors controlling the life and death of cells that form blood vessels (endothelial cells). They showed that endothelial cells rely on a protein called MCL-1 for survival. Potential medications that inhibit MCL-1 are in development, and these may have applications for preventing angiogenesis as a treatment for tumours and certain eye diseases.

Blood vessel formation relies on cell death

The growth and functioning of tissues in our body is dependent on the maintenance of an adequate blood supply. Angiogenesis, the process by which blood vessels are formed, is a highly regulated process in which new vessels are formed and then the vessel system is refined and improved by removing unwanted cells by controlled cell death (apoptosis).

While studying blood vessel development in the retina of the eye, Ms Emma Watson, Dr Leigh Coultas and colleagues revealed an unexpected role for apoptotic cell death during angiogenesis. They showed apoptosis impacts the diameter of capillaries as well as removing 'dead-end' blood vessels that cannot transport blood.

Pinpointing regulators of blood stem cell dormancy

Throughout our lives our bodies maintain a pool of dormant blood stem cells in the bone marrow that can be awakened when needed to produce any type of blood cell.

The dormant state of blood stem cells is controlled by changes to the structure of the cells' DNA and associated proteins – a combination known as chromatin – which regulates access to certain genes. These structural changes are called 'epigenetic' changes.

Associate Professor Anne Voss and Associate Professor Tim Thomas studied the role of two proteins, MOZ and BMI1, in making epigenetic changes to control blood stem cell dormancy. They showed that both proteins were essential not only for maintaining the dormant state of blood stem cells but enabling them to be reactivated when new blood cells are needed.

Health impact

Cancers: bowel cancer, leukaemia, lung cancer, lymphoma, stomach cancer

Immune disorders: inflammatory bowel disease

Other areas: congenital diseases, epigenetics, eye diseases, regenerative medicine, vascular diseases

Division head

Associate Professor Anne Voss

Laboratory heads

Dr Leigh Coultas

Associate Professor Joan Heath

Associate Professor Tim Thomas

11 publications

20 staff

8 students

Associate Professor Tim Thomas (left) and Associate Professor Anne Voss have made the unexpected discovery that blood stem cells are not critical for the day-to-day renewal of the adult blood system.

This finding may lead to new approaches to boosting blood production for people who have been treated with chemotherapy or radiotherapy.

Surprise finding reveals new blood regeneration process

All the cells of our blood are descended from self-renewing blood stem cells. In healthy adults new blood cells are produced every day to replace the cells that are lost through bleeding or the death of damaged cells.

Blood stem cells can be depleted by anti-cancer treatments such as chemotherapy or radiotherapy, and stem cell transplantation is an important method of rebuilding the blood system for some cancer patients.

Associate Professor Tim Thomas, Associate Professor Anne Voss, Dr Bilal Sheikh, Dr Yuqing Yang and colleagues have made a surprising discovery about how blood cells are replenished in healthy adults, which may underpin future advances in therapies that restore depleted blood systems.

"IF WE CAN DEVELOP A WAY TO SWITCH THESE BLOOD-BOOSTING CELLS ON, IT COULD… HELP PEOPLE TO RECOVER MORE QUICKLY FROM CANCER TREATMENTS"

Most research into blood development to date focused on conditions of extreme blood loss, or total ablation of the blood by radiation or chemotherapy, Associate Professor Thomas said. "While those studies provided vital insights that have improved supportive therapies such as stem cell transplantation for people with cancer, they are looking at blood formation in a highly artificial situation," he said.

"We wanted to investigate the 'steady state' process that maintains our blood system throughout adult life, to see whether it was the same as the response to conditions of drastic blood cell loss."

The team made use of a laboratory model they developed in which adult blood stem cells could be specifically deleted, leaving the rest of the blood system intact.

"We were astonished to discover that the entire adult blood system could be maintained for more than one year without blood stem cells," Associate Professor Thomas said.

"This indicates that there are other cells that replenish the blood in the long term. Our hypothesis, which we are now investigating, is that in a normal, healthy situation, blood can be replenished by so-called progenitor cells, very immature blood cells that are descended from stem cells. If this is the case, it will upend long-standing dogma about blood formation and the self-renewal capacity of progenitor cells."

The discovery of a new process by which blood can be replenished could lead to new therapies for people who need their blood system rebuilt, such as cancer patients who have received chemotherapy or radiotherapy.

"If we can develop a way to switch these blood-boosting cells on, it could form the basis of new supportive therapies that help people to recover more quickly from cancer treatments," Associate Professor Thomas said.

Collaborating divisions

Development and Cancer, Cancer and Haematology, Molecular Immunology, Molecular Medicine

Collaborating organisations

Australian Regenerative Medicine Institute, CSIRO, the University of Melbourne

Funding partners

Australian Cancer Research Foundation, Australian National Health and Medical Research Council, Australian Stem Cell Centre, the Victorian Government Operational Infrastructure Support Program

More information

Sheikh BN *et al.* MOZ (KAT6A) is essential for the maintenance of classically defined adult hematopoietic stem cells. *Blood.* 2016 128:2307-2318

Twenty years of cancer research support

A family with one of the most famous names in Australian performing arts has left a generous legacy to the Walter and Eliza Hall Institute.

Managed by Australian Executor Trustees, the estates of Maxwell Gardiner Helpman and Sheila Mary Helpman, along with The Helpmann Family Foundation, have provided more than $3.2 million over the past 20 years to cancer research at the Institute. Their support for the Institute's work highlights not just their generosity but the lives of three prominent Australian artists of the 20th century.

"WE ARE HONOURED TO BE LINKED TO A FAMILY WHO HAS CONTRIBUTED SO RICHLY TO AUSTRALIAN CULTURAL LIFE"

Maxwell and Sheila were the younger siblings of Sir Robert Helpmann, a world-renowned ballet dancer, actor, producer, director and choreographer. Maxwell and Sheila were also active in film and theatre: Maxwell as an actor, director and manager in Canada and Britain; Sheila in theatre, film and television in Britain, Canada and Australia.

The Helpman family has left an extraordinary legacy. Distributions from their estates have contributed to world-class cancer research at the Institute, including advances in treatment for leukaemia, bowel cancer and breast cancer.

Head of Philanthropy at Australian Executor Trustees Mr Ben Clark met with Dr Leigh Coultas, a laboratory head in the Development and Cancer division, on a recent visit to the Institute. Dr Coultas leads a research team investigating the formation of blood vessels, a process called angiogenesis, which is essential for the growth of tumours.

Mr Clark said Australian Executor Trustees supported Australians and their advisers to make a lasting impact through philanthropy. "We are proud to honour the wishes of the Helpman family through supporting the Walter and Eliza Hall Institute of Medical Research and stewarding their perpetual charitable trust," Mr Clark said.

Institute director Professor Doug Hilton said the Helpman family had played an important role in the Institute's history. "The generosity of the Helpman family has had a substantial impact on the Institute's cancer research," Professor Hilton said. "We are honoured to be linked to a family who has contributed so richly to Australian cultural life."

The Institute's cancer researchers have been the beneficiaries of more than $3.2 million in support over the past 20 years from the Helpman estates, managed by Australian Executor Trustees.

Head of Philanthropy at Australian Executor Trustees Mr Ben Clark (centre right) met with cancer researcher Dr Leigh Coultas (left), Institute deputy director Professor David Vaux (centre left) and Institute director Professor Doug Hilton (right).

POPULATION HEALTH AND IMMUNITY

The Population Health and Immunity division uses population-based studies to investigate the basic biology of disease. We have a strong focus on the epidemiology of infectious diseases such as malaria, and understanding the causes of complex diseases including diabetes and brain disorders.

Characterising the *Giardia* stress response

***Giardia* is a gastrointestinal parasite that causes up to 300 million cases of diarrhoea annually. Recent evidence suggests *Giardia* parasites are developing resistance to the most commonly used drug, metronidazole.**

PhD student Mr Brendan Ansell, Associate Professor Aaron Jex and collaborators at the University of Melbourne and the University of Uppsala, Sweden, have investigated how *Giardia* responds to metronidazole, and compared this with its response to two other stresses, high temperatures and exposure to hydrogen peroxide. Their research identified a set of 'stress response' changes in gene usage. The discovery could inform the development of new *Giardia* treatments that target stress response genes, and also enhance the parasite's sensitivity to metronidazole.

Malaria's genetic relatives

Ms Lyndal Henden, a PhD student supervised by Professor Melanie Bahlo, has developed a new algorithm called IsoRelate that improves the evaluation of the relatedness of different genomic samples.

IsoRelate allows comparison of 'diploid' genomes, with two copies of each chromosome, as well as 'haploid' genomes, which have a single copy of each chromosome. One such haploid organism is the stage of the *Plasmodium* parasite that causes malaria in humans.

Ms Henden used IsoRelate to compare the genomes of samples of *Plasmodium falciparum* malaria from people in 14 countries in Africa, South East Asia and the Pacific, providing new insights into the spread of drug resistance, and enabling better monitoring of malaria control efforts.

Detecting 'hidden' malaria infections

***Plasmodium vivax*, the most common malaria parasite in the Asia-Pacific region, can lie dormant in the liver, causing recurring disease and posing a challenge to malaria elimination programs.**

Funding from the Global Health Innovative Technology Fund has enabled Institute researchers, led by Professor Ivo Mueller, to collaborate with partners in Japan, Switzerland, Thailand, Brazil, Papua New Guinea and the Solomon Islands.

The team are developing a diagnostic blood test that detects recent exposure to malaria. This will make it easier to detect and treat carriers of these hidden *P. vivax* parasites, an important step towards elimination of this parasite.

Health impact

Immune disorders: type 1 diabetes, type 2 diabetes

Infectious diseases: filariasis, giardiasis, malaria, tuberculosis, vaccines

Other areas: brain disorders, congenital disease

Division heads

Professor Melanie Bahlo

Professor Ivo Mueller

Laboratory heads

Associate Professor Alyssa Barry

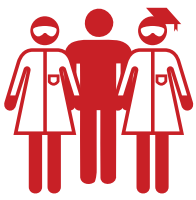
Professor Len Harrison

Associate Professor Aaron Jex

Dr Leanne Robinson

Professor Louis Schofield

70 publications



46 staff

21 students

7 clinicians

Genome technology boosts malaria control efforts

Each year more than 15 million people worldwide experience symptoms of malaria caused by the parasite *Plasmodium vivax*, which is the most common malaria parasite in regions outside of Africa.

P. vivax is becoming increasingly resistant to common antimalarial drugs, posing challenges for malaria elimination in regions including Asia and the Pacific. Associate Professor Alyssa Barry and Professor Ivo Mueller are part of two international teams studying the genetic diversity of *P. vivax*, to understand how it has spread and evolved.

The teams performed the first large-scale genomic analysis of *P. vivax* malaria infections using hundreds of clinical samples from malaria-infected people around the globe.

"WE CAN NOW USE THIS INFORMATION TO STUDY THE CAUSES OF DRUG RESISTANCE AND IMPROVE HOW WE MONITOR THE DISEASE"

The research revealed patterns of variation in the parasite that are the result of both ancient events and recent selection, Professor Mueller said.

"We found that the parasites are remarkably diverse," he said. "The patterns of genetic diversity appear to both result from ancient human migrations and follow more recent historical routes of human movement."

Associate Professor Barry said there were also signs that the parasite population is continuing to evolve in response to recent factors such as drug treatment.

"Drug resistant parasites are firmly established in certain regions, including Indonesia and Papua New Guinea, creating huge challenges for malaria control efforts," she said.

"We found that parasites in these regions have strong genetic signatures of adaptation to antimalarial drugs. We can now use this information to study the causes of drug resistance and improve how we monitor the disease," Associate Professor Barry said.

Parasite diversity within individuals was also examined, revealing that while some people were infected with a single strain of *P. vivax*, other people had more complex, mixed infections with multiple strains of parasites.

"Understanding the diversity of parasites both within an individual and around the globe is an important step towards understanding how malaria is transmitted and in the longer term finding new strategies to control this deadly disease," Associate Professor Barry said.

Collaborating divisions

Population Health and Immunity, Infection and Immunity

Collaborating organisations

Broad Institute of MIT (US), Case Western Reserve University (US), Caucaseco Scientific Research Center (Colombia), Dalian Institute of Biotechnology (China), Indian Council of Medical Research, Institute of Global Health (Spain), Johns Hopkins Bloomberg School of Public Health (US), Malaria Genetic Epidemiology Network partners, National Institute for Public Health (Mexico) New York University (US), Pennsylvania State University (US), Temple University (US), Third Military Medical University (China), Universidad Peruana Cayetano Heredia (Peru), Universidad del Valle (Colombia), University of California San Diego (US), US Navy

Funding partners

Australian National Health and Medical Research Council, Bill & Melinda Gates Foundation, the Medical Research Council (UK), National Institute of Public Health (Mexico), National Institutes of Health (US), Sao Paulo Research Foundation (Brazil), United Kingdom Department for International Development, the Victorian Government Operational Infrastructure Support Program, Wellcome Trust (UK)

More information

Pearson RD *et al*. Genomic analysis of local variation and recent evolution in *Plasmodium vivax*. *Nature Genetics*. 2016 Aug;48(8):953-8

Hupalo DN *et al*. Population genomics studies identify signatures of global dispersal and drug resistance in *Plasmodium vivax*. *Nature Genetics*. 2016 Aug;48(8):959-64

The genetic diversity of *Plasmodium vivax* malaria parasites around the world has been analysed by an international collaborative effort involving Institute researchers including Associate Professor Alyssa Barry. This information may lead to better approaches to monitoring disease spread and improving malaria control.

Searching for new drugs for parasitic diarrhoea

Giardiasis is the most common parasitic cause of diarrhoea globally. It is caused by a gastrointestinal parasite called *Giardia duodenalis*, which infects approximately one billion people worldwide each year.

Repeated or ongoing infections with *Giardia* are a significant cause of malnutrition and failure-to-thrive in children. People who have had giardiasis are also at increased risk of irritable bowel syndrome, chronic fatigue, obesity and diabetes.

> "WE HOPE OUR RESEARCH WILL LEAD TO BETTER DRUGS TO TREAT GIARDIASIS AND STOP PARASITE SPREAD"

Current treatments for *Giardia* are limited and the frequency of drug resistance in the parasite is increasing. Dr Samantha Emery's research aims to develop new drugs to treat *Giardia*, based on a detailed understanding of key molecular processes within the parasite.

A two-year grant from The Jack Brockhoff Foundation has enabled Dr Emery to investigate how drugs can be developed to target a process called lysine acetylation in *Giardia* parasites.

Many proteins within cells are modified by lysine acetylation, Dr Emery said.

"Recent advances in proteomics research have enabled better detection of lysine acetylation, allowing us to align this process with changes in protein functions," she said.

"My research will be the first to characterise which proteins in *Giardia* parasites undergo lysine acetylation. We will then be able to investigate how lysine acetylation impacts *Giardia's* response to current therapies, including whether it contributes to drug resistance."

Compounds that inhibit lysine acetylation have recently emerged as potential new treatments for other parasitic diseases, including malaria.

"In the future we hope our research will lead to better drugs to treat giardiasis and stop parasite spread. We may also be able to identify new combination treatment approaches that can overcome existing drug resistance," Dr Emery said.

Director of The Jack Brockhoff Foundation Professor David Hill AO said the award strengthened research capability in Victoria by helping to establish the careers of talented early-career researchers at a critical time.

"This award supports scientists in demonstrating their originality and capacity to complete a study for publication in scientific literature," Professor Hill said.

Repeated infections with *Giardia duodenalis*, the most common parasitic cause of diarrhoea globally, are a significant cause of malnutrition in children.

Funding from The Jack Brockhoff Foundation is enabling Dr Samatha Emery to investigate potential new treatments for *Giardia*.

TRANSLATION

The Institute is committed to translating fundamental research discoveries into better treatments and preventive approaches for diseases. Collaborations that allow Institute research to develop and enable clinical translation are an important aspect of our work.

More than 100 national and international clinical trials have arisen from Institute research. In 2016 new trials in cancer and immune disorders commenced that have their basis in Institute research discoveries.

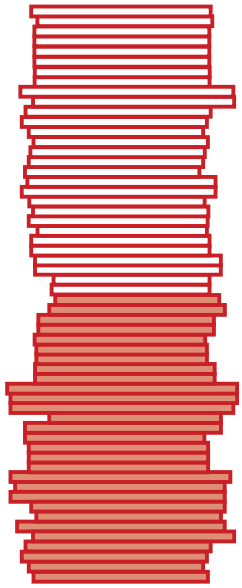
In 2016 Institute researchers collaborated with local, national and international partners from other research organisations, healthcare providers, governmental organisations and industry. Material transfer agreements (MTAs), which enable the sharing of research resources developed at the Institute, are an important starting point of many fruitful and long-term collaborative partnerships. In 2016 the Institute's Business Development Office negotiated MTAs with organisations in 96 countries. The head of Business Development, Dr Julian Clark, is also part of an expert international working group seeking to improve MTAs into the future.

Strong links between our researchers and the clinic are fostered by the Clinical Translation Centre, which supported the research and training of more than 25 clinician-scientists at the Institute. The Consumer Advisory Panel governs and supports the involvement of consumers across the Institute. These consumers are people from varying backgrounds who have experienced the impact of disease and whose skills and knowledge enhance basic research design and create better outcomes for the Institute.

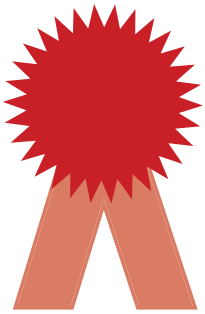
28
consumer buddies
paired with research groups

22
clinician-
scientists

27
PhD students
with medical training



>50%
of publications
related to clinical
translation



44
patents
granted
in 2016

>300
projects

>100
clinical trials

>30
million patients
benefited worldwide

Gold standard for testing anti-cancer agents revealed

A research technique that is widely used to test new anti-cancer agents could be improved by adoption of a worldwide 'gold standard', according to a study led by Institute scientists.

The technique, called 'patient-derived xenografting', is an important way to grow and study cancer samples taken from consenting patients in conditions mimicking the human body. It is widely used for preclinical experiments, such as the testing of new anti-cancer agents, that inform the future development of clinical cancer trials.

> "IN THE LONG TERM, IMPROVING THIS FIELD OF RESEARCH WILL BENEFIT PEOPLE WITH CANCER"

Cancer researchers Dr Kim Pham, Dr Gwo Yaw Ho and Associate Professor Clare Scott led the world-first survey to establish how patient-derived xenografting was conducted and governed by 64 academic research programs in North America, Europe, Australia and Asia.

Dr Pham, who undertook this project as part of her internship in the Business Development Office, said patient-derived xenografts were crucial preclinical research tools. "Worldwide standards for patient-derived xenografts are essential if we are to ensure research in this field can be reproduced and directly compared between laboratories," Dr Pham said.

"Our study uncovered considerable variability in how laboratories around the world undertook these experiments. We have used this to develop a 'gold standard' that we consider to be best practice in the area. The good news is that almost all the laboratories we surveyed had elements of best practice. The next step is for laboratories and organisations overseeing research to develop a process that ensures all laboratories work to the same gold standard," Dr Pham said.

Associate Professor Scott, who is also a medical oncologist at the Peter MacCallum Cancer Centre and The Royal Melbourne Hospital, said gold standard research could be achieved in some situations through research consortia bringing multiple organisations together to collaborate.

"Improvements in reproducibility would enhance international collaborations, as well as accelerating preclinical research output," Associate Professor Scott said.

"We were also able to establish guidelines for how this research can be optimally governed, particularly around questions of how permission for the use and transfer of human samples is governed. In the long term, improving this field of research will benefit people with cancer."

An international study by (from left) Associate Professor Clare Scott, Dr Gwo Yaw Ho and Dr Kim Pham has identified a 'gold standard' for a commonly used laboratory technique for growing human cancer samples.

Targetting the cell death machinery

Cell death is an essential process in our body, removing unwanted and potentially disease-causing cells. Faults in the cell death process have been pinpointed by Institute research as a hallmark of cancer, as well as contributing to a range of immune disorders and infectious diseases.

The Institute's cell death research program spans from basic research into the molecules controlling whether a cell lives or dies, and their relevance to disease, through to drug discovery and trials of new therapeutics that target the cell death machinery.

New leukaemia drug licensed

Venetoclax is a new anti-cancer drug with its foundation in a landmark research discovery made in 1988 by Institute researchers. They found that a protein called BCL-2 promoted cancer cell survival. Ever since then, scientists around the world have been trying to develop strategies to target BCL-2 as a treatment for certain cancers.

Venetoclax binds to BCL-2 and stops it from working, forcing cancer cells to die. The drug was co-developed for use by US pharmaceutical companies AbbVie and Genentech, a member of the Roche group, and was discovered by AbbVie scientists as part of a joint research collaboration with Walter and Eliza Hall Institute scientists.

Institute researchers were heavily involved in the very first clinical trials of venetoclax.

In 2016 venetoclax was approved for use in the United States and European Union. In January 2017, the drug (marketed as VENCLEXTA™) was also approved for use by the Australian Therapeutic Goods Administration and made available to Australian patients with high-risk forms of chronic lymphocytic leukaemia.

Partnership shows hope for new anti-cancer compound

A collaborative partnership between the Institute and international company Servier has facilitated the development of a new compound that shows promise in treating multiple human cancers.

The compound S63845 targets the BCL-2-like cell survival protein MCL-1, which is essential for the sustained growth of up to a quarter of all cancers. S63845 was discovered jointly by Servier, headquartered in France, and Vernalis (R&D), based in the UK.

Walter and Eliza Hall Institute scientists, collaborating with researchers at The Alfred Hospital and Servier, demonstrated that S63845 was not only effective against several cancer types, but that it could also be delivered at doses that were well tolerated by normal cells.

An ongoing collaboration on this target class between Servier and the pharmaceutical company Novartis is now working towards clinical development of a MCL-1 inhibitor.

Broadening the focus on cell death

In addition to investigating how cell survival is controlled by BCL-2-like proteins, Institute scientists are also unravelling alternate mechanisms for regulating cell death, and their relevance to a range of diseases.

One area of focus is on cell death driven by SMAC, a protein that was jointly discovered at the Institute in the 1990s. A drug called birinapant, which acts like SMAC to kill cells, is being investigated for treating cancer as well as certain chronic infectious diseases. Birinapant was developed by TetraLogic Pharmaceuticals and is being clinically evaluated by Swedish oncology company Medivir AB.

Institute research underpinned clinical trials of birinapant for treating chronic hepatitis B, an incurable viral infection that causes more than 500,000 deaths worldwide each year.

Institute research has also extended to less well-understood forms of programmed cell death, including a process called necroptosis. Institute scientists have demonstrated how this process is regulated at the molecular level, as well as beginning to investigate how inflammatory diseases and cancer might be treated with drugs that modulate necroptosis.

Understanding the three-dimensional molecular structure of proteins is a key step in the development of new agents that modify the proteins' function.

Dr Peter Czabotar has used structural biology to create atomic-level maps of proteins involved in cell death processes including necroptosis. This may lead to better treatments for inflammatory diseases and cancer.

Harnessing the power of the immune system

Our immune system is comprised of a complex network of cells that functions to keeps us healthy.

Many diseases occur either because rogue immune cells attack our own tissues, or because diseased cells or microbes are able to escape or evade our immune defences.

As well as having a strong focus on fundamental immunology research, many of our scientists are investigating how immune cells can be modified to prevent or fight diseases – a field called immunotherapy.

"WE CAN NOW USE THIS INFORMATION TO IMPROVE THE ABILITY OF CANCER PATIENTS' NK CELLS TO FIGHT CANCERS SUCH AS MELANOMA"

Institute researchers have been making advances in understanding how our immune system can be harnessed to fight cancer, focusing on many different cancer-fighting cell types and therapeutic approaches.

One aspect of this has been to investigate how the cancer-fighting abilities of natural killer (NK) cells can be enhanced, to increase their ability to destroy tumour cells.

Research led by Dr Sandra Nicholson and Dr Nick Huntington revealed a protein 'brake' in NK cells that restrains their ability to attack cancer cells.

Dr Nicholson said the team was investigating how immune cells, such as NK cells, could be modified to prevent or fight disease.

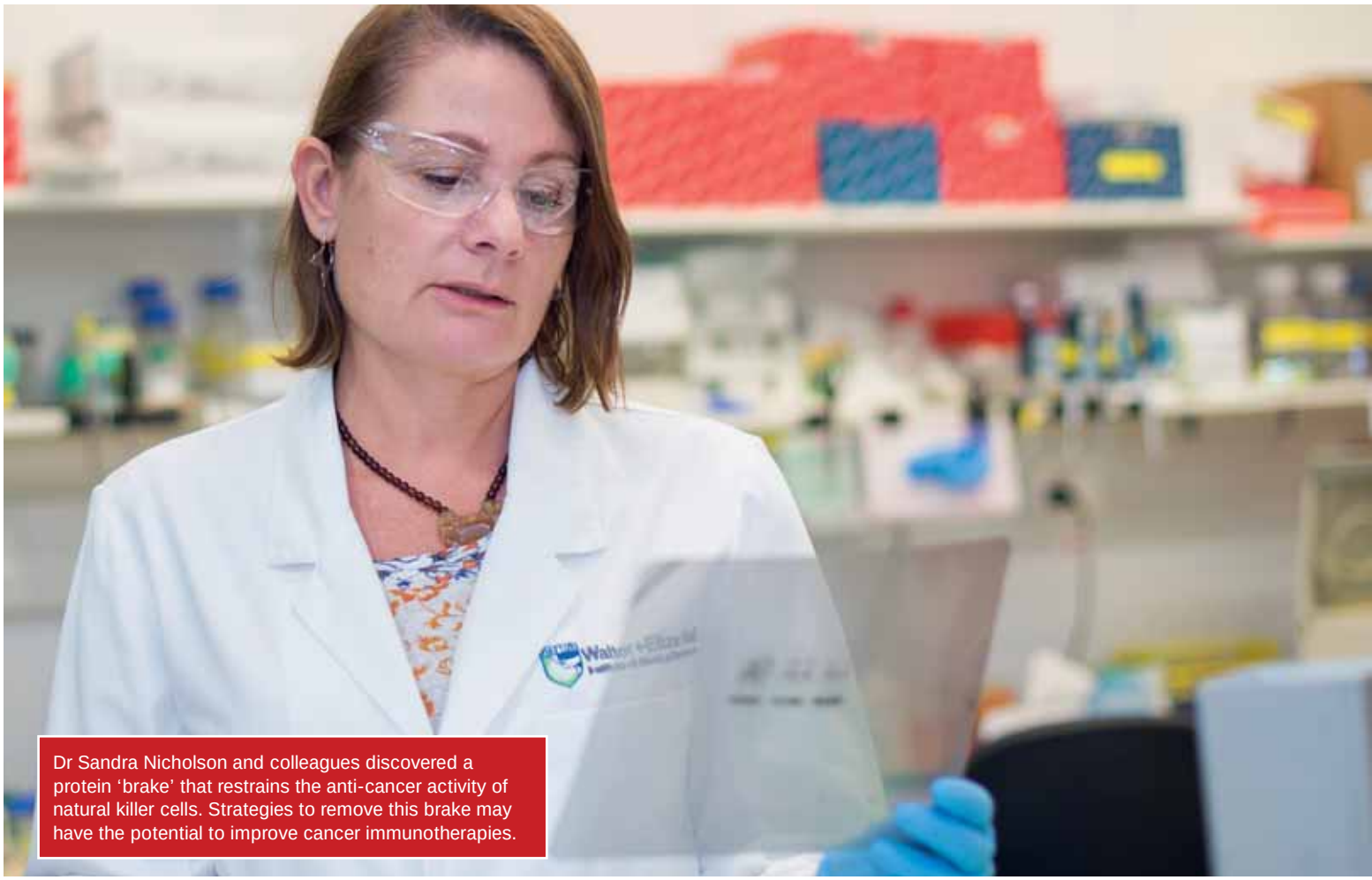
"We showed in an experimental model that when the brake was removed, NK cells were better able to protect the body against metastatic melanoma," Dr Nicholson said.

"By identifying how this protein inhibits NK cell responses, we can now use this information to improve the ability of cancer patients' NK cells to fight cancers such as melanoma."

Cancer immunotherapy had received considerable interest in recent years, because of the successes seen with recent clinical trials.

Dr Huntington said the team was now working to identify potential drugs that could enhance NK cell activity in cancer patients.

"We are hopeful our research will lead to new cancer immunotherapies that supercharge the body's NK cells, and maintain them in this state to efficiently and specifically fight cancer," Dr Huntington said.



Dr Sandra Nicholson and colleagues discovered a protein 'brake' that restrains the anti-cancer activity of natural killer cells. Strategies to remove this brake may have the potential to improve cancer immunotherapies.

Decades of research underpin new clinical trial

Around 250,000 Australians are affected by rheumatoid arthritis, a chronic and incurable inflammatory disease that is caused by the immune system attacking joints and other tissues.

For more than two decades a team of Institute researchers led by Professor Ian Wicks have been probing how inflammatory conditions such as rheumatoid arthritis develop. Commercial partnerships are now seeing this research enter clinical trials.

"THROUGH INDUSTRY COLLABORATIONS WE HAVE BEEN ABLE TO PURSUE THE TRANSLATION OF THESE FINDINGS INTO SEVERAL POTENTIAL NEW THERAPEUTICS"

An important focus of Professor Wicks' investigations has been the role of cell signalling hormones called colony stimulating factors (CSFs) in driving inflammation. CSFs were first discovered at the Institute by Professor Don Metcalf and his colleagues in the 1960s.

Professor Wicks, who is also head of Rheumatology at The Royal Melbourne Hospital, said the team's preclinical research had pinpointed two CSFs, G-CSF and GM-CSF, as potential therapeutic targets for treating a variety of autoimmune diseases.

"Through industry collaborations, in particular with Australian biopharmaceutical company CSL, we have been able to pursue the translation of these findings into several potential new therapeutics," Professor Wicks said.

In 2016 CSL324, a monoclonal antibody that neutralises G-CSF, began a world first phase 1 clinical trial for the treatment of inflammatory diseases.

A monoclonal antibody that neutralises GM-CSF, developed by CSL and MedImmune, a subsidiary of AstraZeneca, has also progressed into late stage clinical development.

Dr Andrew Cuthbertson, CSL's chief scientific officer, said research into CSFs in inflammatory diseases was an excellent example of the strength of Australian medical research. "The development of CSL324 to date is another fine example of the power of collaboration and speaks to the outstanding quality of science in Australia's medical research institutions. We look forward to continuing work on the drug as it moves through the phase 1 clinical trial," he said.

The Institute's rheumatoid arthritis research has benefited from the long-term philanthropic support of the John T Reid Charitable Trusts.

Autoimmunity pinpointed as a cause of hives

Urticaria, also known as 'hives' – itchy, raised welts in the skin – is a condition that affects about one in five Australians at some stage of their lives.

Clinical immunologist and PhD student Dr Priscilla Auyeung, in collaboration with Professor Len Harrison, Dr Diana Mittag and Professor Phil Hodgkin, has investigated whether immune T cells are involved in causing chronic spontaneous urticaria (CSU). People with this condition experience recurring hives for at least six weeks, and usually much longer, for no apparent reason.

Dr Auyeung said people with CSU found it very frustrating that the trigger for the condition was not known.

"Patients often think that they're allergic to their washing powder, soap or shampoo, and sometimes even wonder if it is all in their mind," she said.

Using samples from CSU patients attending The Royal Melbourne Hospital, Dr Auyeung was able to investigate what triggers the T cells that cause hives.

"THIS ABERRANT AUTOIMMUNE T CELL ACTIVATION UNDERPINS THE INFLAMMATION THAT CAUSES ITCHY HIVES"

"Our research found that in the majority of people with CSU, T cells react to a specific protein antigen that occurs on other immune cells. This aberrant autoimmune T cell activation underpins the inflammation that causes itchy hives," she said. "Since the 1980s there had been speculation that CSU had an autoimmune basis, and our research has cemented the role of autoimmune T cells in this condition."

"We hope that the insights we have gained into the immune mechanism of CSU could be the foundation for new, targeted treatments for this condition," Dr Auyeung said.

People with chronic spontaneous urticaria experience recurring itchy hives with no apparent trigger.

The discovery of the immune mechanism causing chronic spontaneous urticaria by Dr Priscilla Auyeung and colleagues could lay the foundation for new, targeted treatments for this condition.

Malaria vaccines on the horizon

More than 30 years of malaria research at the Institute has culminated in the development of two potential malaria vaccines that are showing great promise in the battle to prevent – and potentially eradicate – malaria.

Bridging the GAP

The GAP vaccine is a live attenuated vaccine against *Plasmodium falciparum*, the most deadly form of malaria.

Dr Priyanka Sathe, who manages the GAP vaccine project, said the vaccine used a 'disarmed' parasite stripped of its ability to evade immune detection – a key part of its survival strategy.

"The vaccine has knocked out the parasite's mechanism of hiding from the immune system, by interfering with the parasite's ability to bind blood vessel walls within organs," Dr Sathe said. "This means more parasites come into contact with immune cells, and we anticipate this will result in a much more effective immune response and faster clearance of the parasite, while also generating long-term immunity."

The GAP vaccine will soon go into phase 1 clinical trials, in a collaboration between the Walter and Eliza Hall Institute and the QIMR Berghofer Medical Research Institute. The trial will assess the safety of the vaccine, while also studying how the immune system responds to the vaccine.

The GAP vaccine is particularly focused on disrupting the blood stage of *P. falciparum* malaria infection, which is the stage where the classical malaria symptoms occur, and can quickly lead to severe illness and death.

Dr Sathe said the live attenuated vaccine, which was created at the Walter and Eliza Hall Institute, could also be used as a platform technology for vaccines.

"This strategy has previously shown great immune responses in laboratory models," Dr Sathe said. "If it proves true in humans we will be excited to investigate whether it could be a suitable delivery system for protecting against other types of malaria, or even other diseases," Dr Sathe said.

One vaccine to eradicate all malaria

A second vaccine in development has a unique approach to tackling malaria: it targets a carbohydrate known as GPI that is essential for all malaria parasites.

The GPI vaccine is in preclinical development through a collaboration between the Walter and Eliza Hall Institute and James Cook University.

Professor Louis Schofield, who first had the idea to target the GPI molecule 30 years ago and is leading the research project, said the vaccine was unusual because it targeted a carbohydrate, not a protein.

"Traditionally, carbohydrate-based vaccines tend to be less effective because it is hard to convince the immune system to attack a carbohydrate the same way that it will attack a protein," he said. "However GPI is a critical malaria vaccine candidate, and we have developed a vaccine that can successfully produce an immune response and we are now refining and optimising it for future clinical trials."

Professor Schofield said the most exciting aspect of the GPI vaccine was its ability to target any strain of the malaria parasite, at any stage of its lifecycle.

"This vaccine is unique because it meets all the features that are internationally agreed to be essential for a vaccine that will contribute to malaria eradication," Professor Schofield said.

Associate Professor Harin Karunajeewa is a clinician-scientist whose research aims to improve drug treatments for globally significant infectious diseases including malaria, tuberculosis, pneumonia and gastrointestinal disease.

Improving the detection of acute rheumatic fever

Acute rheumatic fever is a serious inflammatory disease triggered by infection with group A streptococcus bacteria. Recurring or lengthy bouts of this disease can permanently damage the heart valves, leading to a condition called rheumatic heart disease.

The prevalence of acute rheumatic fever is disproportionately high in Aboriginal and Torres Strait Islander Australians, particularly in children living in remote communities. Rheumatic heart disease is a significant cause of illness and death amongst young adults in these communities; worldwide more than 300,000 people die from the condition each year.

"IMPROVEMENTS IN THE EARLY DETECTION OF ACUTE RHEUMATIC FEVER HAVE THE POTENTIAL TO REDUCE THE HEALTH BURDEN OF THIS DEBILITATING DISEASE"

Dr Laura Dagley, Dr Giuseppe Infusini and Dr Andrew Webb from the Institute's proteomics laboratory are developing a diagnostic test for acute rheumatic fever that could potentially be used in remote Australian communities.

Dr Dagley said there was currently no definitive method for diagnosing the disease, and misdiagnosis was a common and significant contributor to the high rates of rheumatic heart disease seen in Aboriginal Australians.

"The diagnosis of acute rheumatic fever today mainly relies on symptoms including joint inflammation, fever and heart issues – and this has not changed much in the past 50 years," she said.

Dr Dagley is leading research that aims to discover 'biomarkers', or changes in proteins, that could be used to diagnose acute rheumatic fever.

The team measured thousands of proteins in blood samples from children with acute rheumatic fever, and identified a protein 'signature' that will be evaluated as a diagnostic test for the disease.

"In the next phases of the project we will be broadening our testing of patient samples to determine whether we can consistently diagnose acute rheumatic fever by this signature, bringing us one step closer to our goal of developing a reliable diagnostic test," Dr Dagley said.

"Improvements in the early detection of acute rheumatic fever have the potential to reduce the health burden of this debilitating disease in Aboriginal and Torres Strait Islander communities."

Scabies genome gives clues for disease control

The scabies mite is a parasite responsible for serious health problems in people living in remote Aboriginal communities, affecting one in two children and one in four adults each year.

The parasite causes extremely itchy skin infestations that often become infected, causing serious – and even lifelong or fatal – complications, such as bacterial blood infection and sepsis. Scabies is also associated with serious kidney and heart diseases, including rheumatic heart disease.

A research team led by Institute researcher Associate Professor Tony Papenfuss and Dr Katja Fischer from the QIMR Berghofer Medical Research Institute has sequenced the genome – or 'genetic map' – of the human scabies mite.

The team hopes this advance could accelerate research that underpins new ways of preventing and treating scabies infestations and their lifelong complications.

Genomic technologies are critical for finding ways to prevent and control scabies, Associate Professor Papenfuss said. "Prior to this study, little was known about the genetic makeup of the scabies mite," he said.

"Understanding the genetic makeup of the scabies mite will help to identify how it becomes resistant to certain drugs and could suggest new strategies for development of novel therapeutics."

"PRIOR TO THIS STUDY, LITTLE WAS KNOWN ABOUT THE GENETIC MAKEUP OF THE SCABIES MITE"

The team compared DNA sequences from human scabies mites with those from domestic pigs, which commonly have scabies.

"One of the unexpected things we found was that one patient was infected with mites that were genetically more similar to pig mites than to human mites," Associate Professor Papenfuss said.

"This suggests it may be possible for certain animal strains of mite to infect humans, which we did not previously know was possible. If subsequent studies confirm this finding, it could have major implications for disease control programs."

Dr Laura Dagley is using proteomics to develop a blood-based test to detect acute rheumatic fever, an inflammatory disease which disproportionately affects Aboriginal and Torres Strait Islander Australians.

Dr Dagley's research achievements were celebrated with her selection as a finalist in the 2016 Bupa Health Foundation Emerging Health Researcher Awards.

Dr Belinda Lee is a clinician-scientist at the Institute and a medical oncologist at Victorian Comprehensive Cancer Centre partners The Royal Melbourne Hospital and the Peter MacCallum Cancer Centre. The Philip Hemstritch Centenary Fellowship is supporting Dr Lee's research into better treatments for pancreatic cancer.

Victorian Comprehensive Cancer Centre alliance boosts cancer research

The Victorian Comprehensive Cancer Centre (VCCC) is a powerful alliance of leading Victorian hospitals and research centres, including the Walter and Eliza Hall Institute, which are committed to controlling cancer.

VCCC partner organisations celebrated a milestone on 17 July 2016, with the new purpose-built VCCC facility in Parkville opened by the Victorian Premier, the Hon. Daniel Andrews MP; the Victorian Health Minister, the Hon. Jill Hennessey MP; and the Australian Health Minister, the Hon. Sussan Ley MP.

On the same day United States Vice President Joe Biden, who championed the US Cancer Moonshot initiative, toured the new building and announced a memorandum of understanding between the National Cancer Institute, US, and the state of Victoria to enhance knowledge sharing and cooperation in cancer research.

The $1.1 billion VCCC facility, which has enabled the relocation of the Peter MacCallum Cancer Centre, brings new clinical and translational opportunities to the Parkville precinct. The VCCC partnership has also fostered new and strengthened collaborative links between the Institute and its VCCC partner organisations, accelerating advances in cancer prevention, diagnosis, treatment and education.

The Institute is a founding partner and the research powerhouse of the VCCC, and many Institute researchers contribute to the alliance's leadership and governance, or hold joint appointments across partner organisations.

In 2016, the Institute's head of Clinical Translation, Professor Andrew Roberts, was appointed the chair of the VCCC's Cancer Research Advisory committee, which helps to guide the alliance's translational research focus. Professor Roberts is also the University of Melbourne Metcalf Chair of Leukaemia Research and a member of the integrated clinical haematology department of the Royal Melbourne Hospital and the Peter MacCallum Cancer Centre.

Professor Roberts and Associate Professor Peter Gibbs, a clinician-scientist at the Institute and medical oncologist, have been named VCCC Research and Education leads – Professor Roberts for the haematology tumour stream, and Associate Professor Gibbs for gastrointestinal cancers.

Australia-China joint venture to fast-track discoveries

The past 25 years have witnessed the emergence of China as an economic and intellectual powerhouse, including significant growth in its biomedical research capacity.

The Institute's strong research track record, particularly in translating laboratory research into the clinic, has enabled successful engagement with leading researchers and research institutions in China.

In September 2016, Victorian Premier the Hon. Daniel Andrews MP announced plans to establish a translational medicine centre in Nanjing, following the signing of a memorandum of understanding between the Walter and Eliza Hall Institute, the University of Melbourne, Cancer Trials Australia and China's Nanjing University.

Building on early collaborative work from LaTrobe University, this powerful four-way alliance is committed to advancing an innovative translational research centre with a focus on cancer, inflammation and infectious disease.

Professor Hilton said the centre would be a platform for the exchange of expertise and resources, with unparalleled opportunities for collaboration.

"The centre will generate accessible preventions and treatments, building on Melbourne's reputation as a world leader in translational medicine," Professor Hilton said.

University of Melbourne vice-chancellor Professor Glyn Davis said the venture offered outstanding opportunities for biomedical research in Victoria.

"We are confident the collaboration will offer our students and academic researchers unique opportunities to excel with academic partners in China," Professor Davis said.

Chair of Cancer Trials Australia Professor Andrew Scott said it was clear the partnership would evolve into a greater involvement with scientists and clinicians, and the emerging Chinese biotechnology and capital sectors.

"By combining expertise in first-in-human trials and in larger patient cohort trials, with skills in bioinformatics, genomics, biology and medicinal chemistry, the partnership will accelerate developments in the area of personalised medicine," Professor Scott said.

‘Cellular CCTV’ solves leukaemia mystery

New imaging technologies and increasingly powerful computing resources are allowing Institute researchers unprecedented views of how the body works.

Dr Edwin Hawkins, in collaboration with Dr Cristina Lo Celso from Imperial College London, UK, has used a revolutionary high-resolution imaging technique to solve a longstanding mystery of how leukaemia cells resist and retaliate against chemotherapy.

> “AS A VIDEO-BASED MEDIUM, WE COULD WATCH ACTION UNFOLDING FOR DAYS, WITH THE ABILITY TO ZOOM IN AND OUT ON THE SAME PATCH OF TISSUE FROM SEVERAL MILLIMETRES RIGHT DOWN TO A SINGLE MICRON”

Leukaemia is a type of blood cancer with significantly high mortality rates. In Australia, half of adult leukaemia patients relapse after their initial chemotherapy treatment. Often resistant to subsequent treatments, the cancer progresses and becomes fatal.

Dr Hawkins and Dr Lo Celso employed a new imaging technology, termed ‘optical windows’, that enabled them to observe leukaemia cells’ response to chemotherapy – a virtual ‘cellular CCTV’.

Dr Hawkins said previous imaging techniques could only capture static ‘snap-shots’, whereas the new technique was far more dynamic.

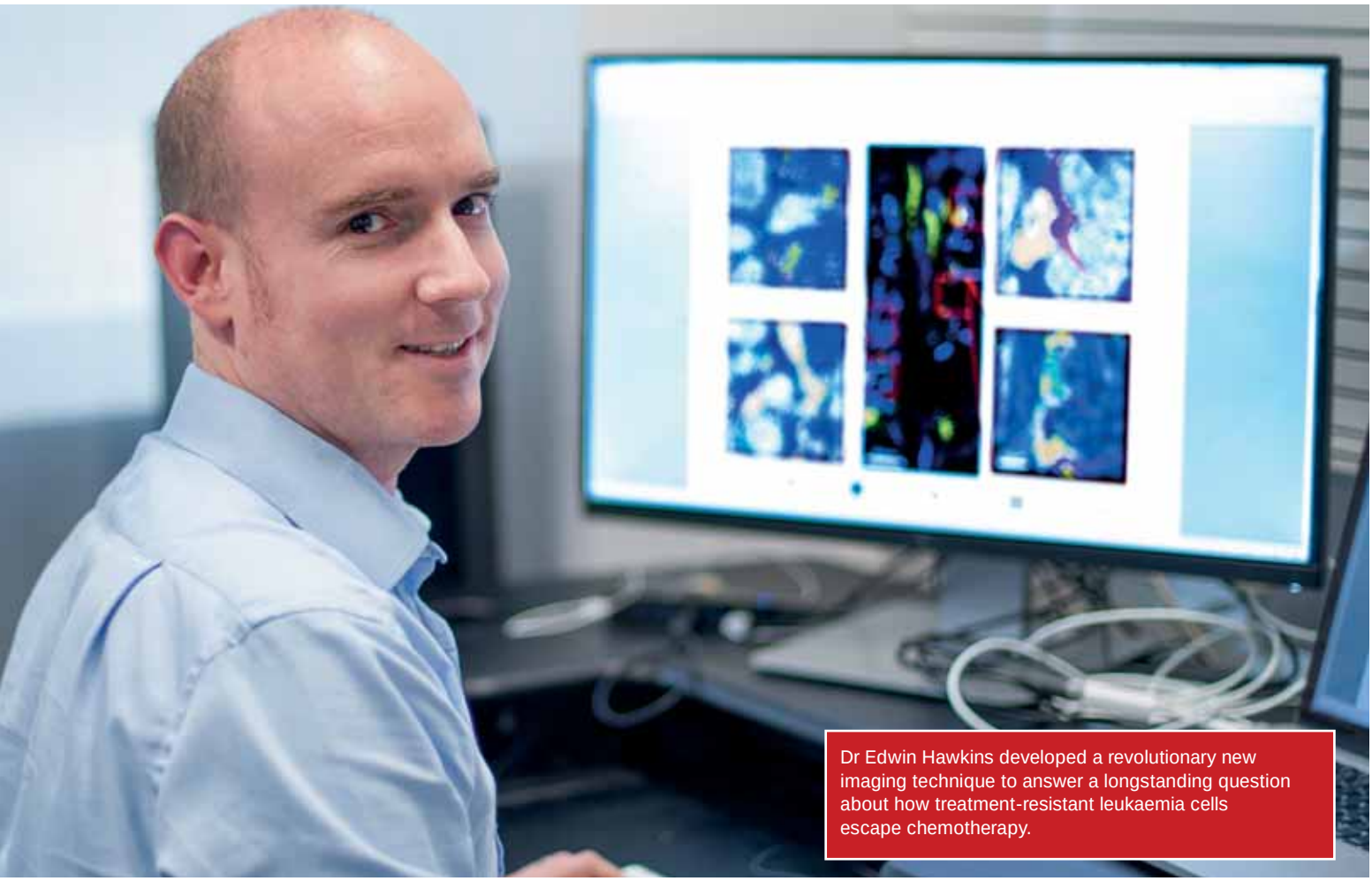
“As a video-based medium, we could watch action unfolding for days, with the ability to zoom in and out on the same patch of tissue from several millimetres right down to a single micron,” Dr Hawkins said.

The research, published in the journal *Nature*, overturned the conventional theory that acute lymphoblastic leukaemia (ALL) cells resist cancer treatment by ‘hiding’ in the bone marrow.

Dr Hawkins said he was surprised to find that treatment-resistant cells were doing the exact opposite of ‘hiding’ in order to survive. “Instead of playing ‘hide-and-seek’ with the chemotherapy, as was the widely-held belief, treatment-resistant ALL cells were engaging in a game of ‘tag’ with the immune system and running riot around the body,” he said.

Dr Lo Celso said this revelation would mean a shift in focus for researchers working to advance treatments for ALL.

“We now know that it is ineffective to design treatments to target the surrounding stromal cells or ‘hiding places’,” Dr Lo Celso said.



Dr Edwin Hawkins developed a revolutionary new imaging technique to answer a longstanding question about how treatment-resistant leukaemia cells escape chemotherapy.

PATENTS GRANTED IN 2016

Immunogenic compositions and uses thereof
Inventors: L Schofield
Canada

Therapeutic molecules and methods for generating and/or selecting same
Inventors: P Colman, D Fairlie, D Huang, E Lee
Europe, UK, Ireland, France, Germany, Switzerland, The Netherlands, Denmark, Sweden

Structure of the insulin receptor ectodomain
Inventors: T Adams, T Garrett, M Lawrence, L Meizhen, G Lovrecz, N McKern, L Sparrow, V Streltsov, C Ward
Belgium, France, Germany, Ireland, Italy, The Netherlands, Sweden, Switzerland, UK

Methods and compositions for treating and preventing malaria (2)
Inventors: J Beeson, A Cowman, S Lopaticki, A Maier, K Persson, J Richards
Canada

Methods of detecting cells with a disrupted cell membrane, cells infected with a pathogen, dying cells or dead cells
Inventors: I Caminschi, D Huang, M Lahoud, K Shortman, M Van Delft, M Wright, J Zhang
Europe, Israel

Barley with low levels of hordeins
Inventors: C Howitt, G Tanner
Canada, Japan

Compositions and methods for treatment of celiac disease
Inventors: B Anderson
US

Compounds and methods of use (ureas)
Inventors: J Baell, C Bui, P Colman, P Czabotar, D Danette, S Elmore, W Fairbrother, J Flygare, G Lessene, C Ndubaku, G Nikolaopoulos, A Petros, C Rye, B Smith, A Souers, K Watson
South Korea, The Philippines, France, Germany, Italy, Spain, UK

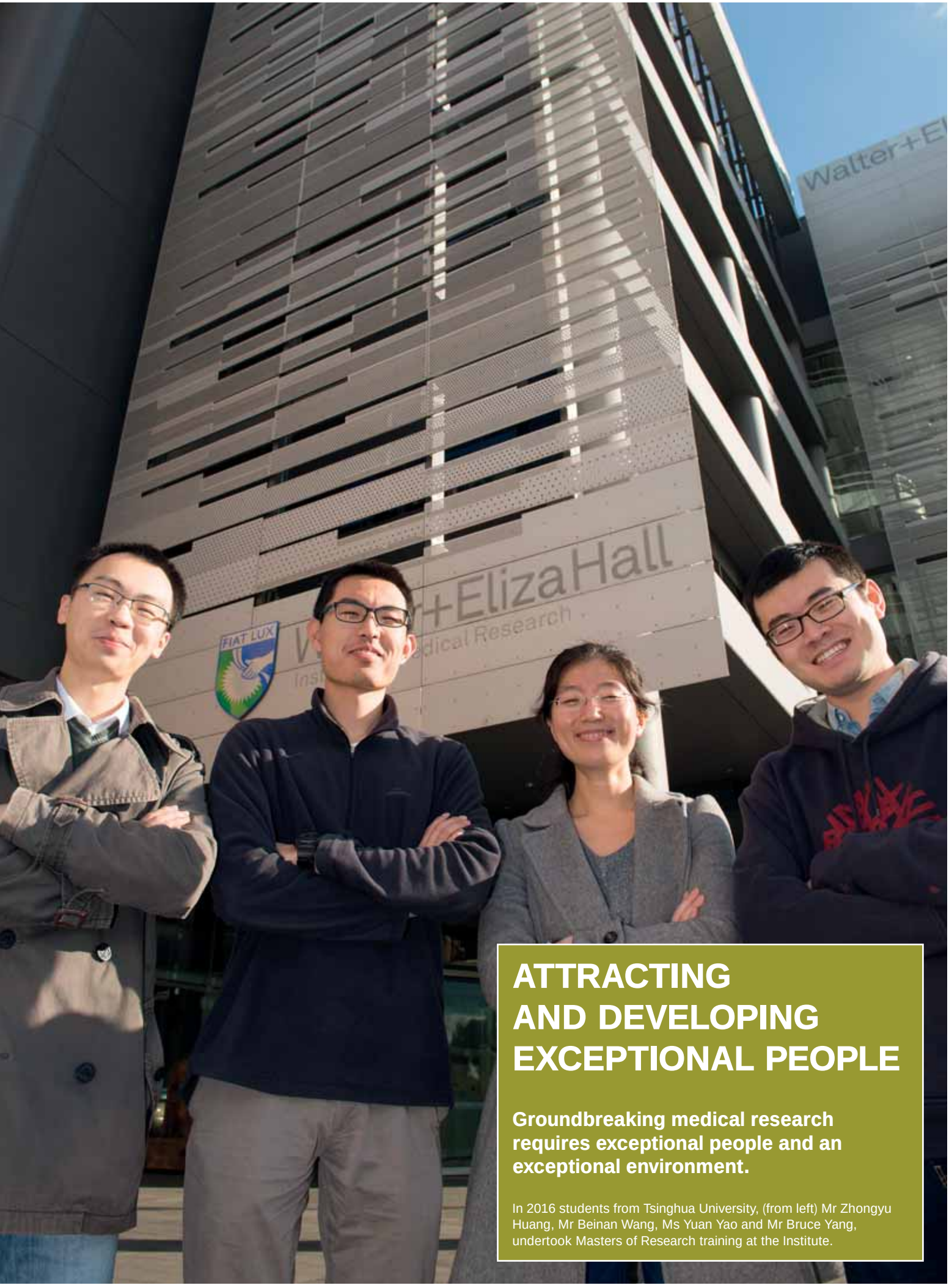
Compounds and methods of use (amides)
Inventors: J Baell, C Bui, P Colman, P Czabotar, D Danette, S Elmore, W Fairbrother, J Flygare, L Hasvold, G Lessene, C Ndubaku, G Nikolaopoulos, A Petros, C Rye, B Smith, A Souers, Z Tao, L Wang, X Wang, K Watson
South Korea, Ukraine

Soluble mediator
Inventors: E Bandala Sanchez, J Dromey, L Harrison, M Rashidi, Y Zhang
China, Japan

Novel anti-cancer agents
Inventors: T Burgess, G Lessene, F Walker, K Watson, H Witchard
China, US, Europe

Apoptosis-inducing agents for the treatment of cancer and immune and autoimmune diseases
Inventors: M Bruncko, Y Dai, H Ding, G Doherty, L Hasvold, L hexamer, A Kunzer, R Matei, W McClellan, S Moore, C Park, C park, A Petros, X Song, A Souers, G Sullivan, Z Tao, L Wang, G Wang, M Wendt
Australia, China, Indonesia, South Korea, Japan

Apoptosis inducing agents for the treatment of cancer and immune and autoimmune diseases
Inventors: M Bruncko, H Ding, G Doherty, S Elmore, L Hasvold, L Hexamer, A Kunzer, X Song, A Souers, G Sullivan, Z Tao, L Wang, G Wang, X Wang, M Wendt, R Mantei, T Hansen
US



ATTRACTING AND DEVELOPING EXCEPTIONAL PEOPLE

Groundbreaking medical research requires exceptional people and an exceptional environment.

In 2016 students from Tsinghua University, (from left) Mr Zhongyu Huang, Mr Beinan Wang, Ms Yuan Yao and Mr Bruce Yang, undertook Masters of Research training at the Institute.

EDUCATING THE NEXT GENERATION

Students InSPIRE research collaboration between Australia and China

In 2016, the Institute's International Student Program in Research Experience (InSPIRE) welcomed undergraduate students from leading universities in China.

The inaugural program brought 12 talented students – selected from Fudan University, Nanjing University, Nankai University and Tsinghua University – to Melbourne on a fully funded 10-week internship.

The students gained research experience through one-on-one mentorship in a broad range of biomedical research areas including computational biology, biological imaging and biochemistry.

The InSPIRE program lead Dr Grant Dewson said the initiative was central to the Institute's strong spirit of international collaboration.

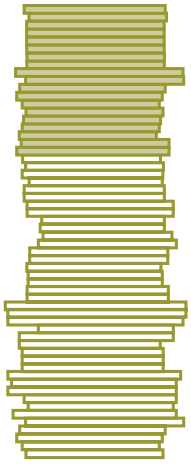
"Australia is a world-class destination for biomedical education and the InSPIRE program offers students the opportunity to foster new and long-standing collaborative ventures with some of Australia's leading medical research teams," Dr Dewson said.

Institute director Professor Doug Hilton said it was exciting to see the interns joining the Institute's research teams working to understand, prevent and treat cancers, immune disorders and infectious disease.

"THE INSPIRE PROGRAM OFFERS STUDENTS THE OPPORTUNITY TO FOSTER NEW AND LONG-STANDING COLLABORATIVE VENTURES WITH SOME OF AUSTRALIA'S LEADING MEDICAL RESEARCH TEAMS"

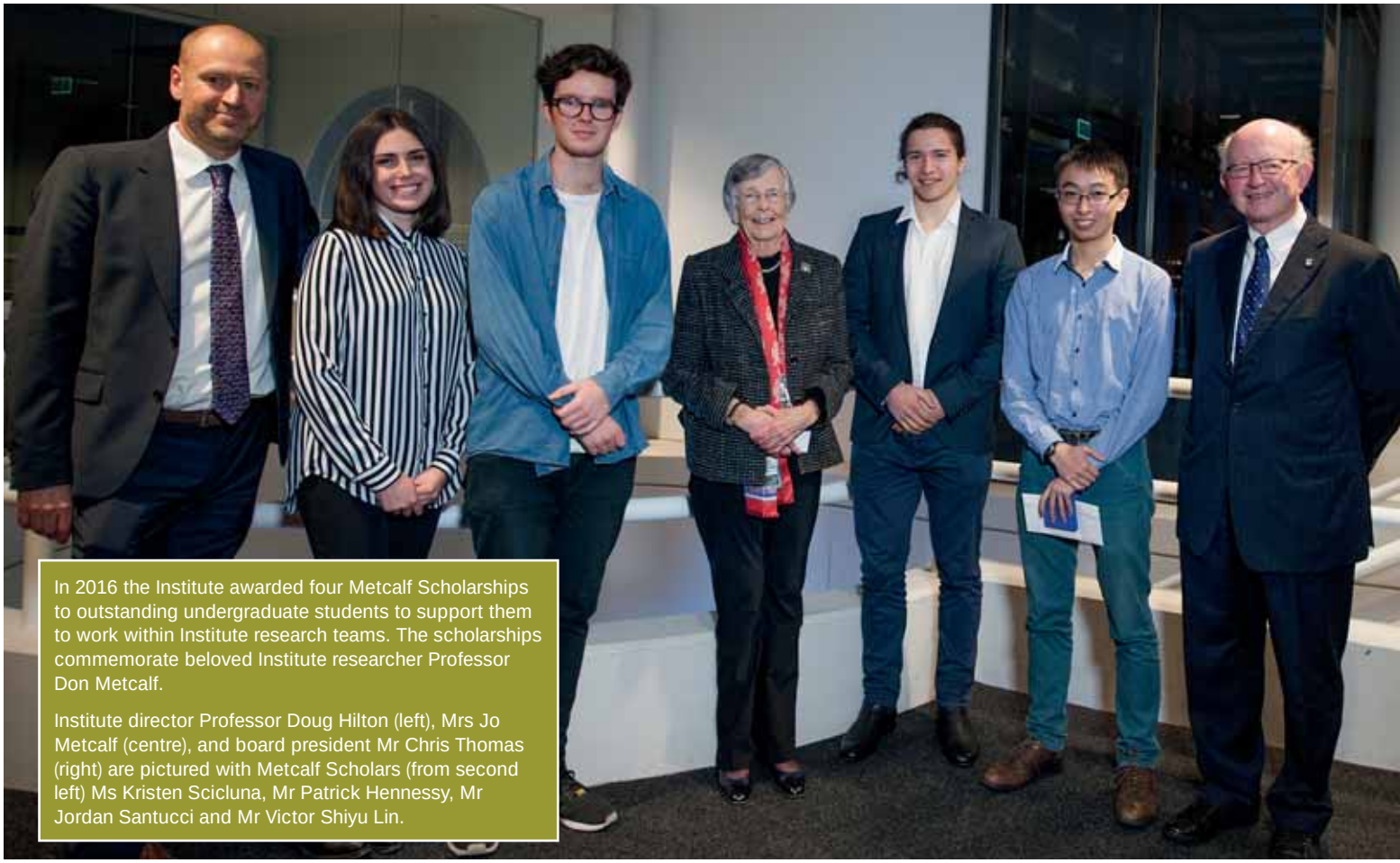
"The students were warmly welcomed into the Institute family and were provided every opportunity to develop a passion for medical research and make discoveries for humanity," Professor Hilton said. "We look forward to maintaining connections with these outstanding researchers as Institute alumni."

225
students



25
publications with student authors with impact factor >10

89
publications with student authors



In 2016 the Institute awarded four Metcalf Scholarships to outstanding undergraduate students to support them to work within Institute research teams. The scholarships commemorate beloved Institute researcher Professor Don Metcalf.

Institute director Professor Doug Hilton (left), Mrs Jo Metcalf (centre), and board president Mr Chris Thomas (right) are pictured with Metcalf Scholars (from second left) Ms Kristen Scicluna, Mr Patrick Hennessy, Mr Jordan Santucci and Mr Victor Shiyu Lin.

Following the fate of disease-fighting T cells

T cells are a critical component of our immune defences, orchestrating protective and long-lasting immunity to infections. Faulty T cells can also launch misdirected attacks on our body's own tissues, causing autoimmune diseases such as type 1 diabetes and rheumatoid arthritis.

T cells are produced by the thymus, with each cell 'pre-programmed' to recognise a unique molecule. Should that molecule be part of a virus or bacterium invading the body, it will activate the corresponding T cell. The cell will then divide multiple times to generate an army of T cells that launch an immediate immune response, but also produce 'memory' cells that provide long-term protection.

"MY YEAR AT THE INSTITUTE HAS BEEN A FORMATIVE EXPERIENCE"

Mr Miles Horton's honours research examined how T cells acquire their disease-fighting functions when they become active. Working with Dr Susanne Heinzel and Professor Phil Hodgkin, Mr Horton used a novel fluorescent cell labelling technique that allowed him to follow the fate of individual T cells and their progeny through several rounds of cell division.

The research helped to explain how armies of T cells inherit certain traits from their parent cell, Mr Horton said. "We now have a better understanding of how T cells operate to achieve the remarkable level of diversity required for effective immune responses," he said.

"In the long term, this research may contribute to treatments that harness the immune system to treat infections or diseases such as cancer and autoimmunity."

Mr Horton received the Colman Speed Medal as the top honours student at the Institute, and also achieved the highest academic performance in the Bachelor of Biomedicine Honours course at the University of Melbourne in 2016.

He said his honours placement was his first experience of laboratory research. "My year at the Institute has been a formative experience," Mr Horton said. "The opportunity to learn how to rigorously design experiments and interpret data was deeply rewarding.

"It was also thoroughly enjoyable to learn from a wide array of talented scientists at the Institute. The willingness of staff and students to dedicate their time and expertise to help others learn is a great attribute of Institute life."

Mr Horton's next step is to commence a medical degree at the University of Melbourne, but it won't take him far from the laboratory. "I'm planning to continue to collaborate with Institute researchers during my studies," he said. "I hope to become a clinician-scientist in a field such as immunology or haematology."

T cells are an important component of our immune system. Honours student Mr Miles Horton (right), who was supervised by Dr Susanne Heinzel (left) and Professor Phil Hodgkin, discovered how T cells acquire infection-fighting functions during an immune response.

Explaining the causes of immune deficiencies

Primary immune deficiencies are conditions in which a person has a weakened response to infections. In many cases this is caused by a genetic change. This leaves the person vulnerable to more frequent and severe infections than other people, but also, paradoxically, may cause other elements of the immune system to launch autoimmune attacks on the body's own tissues.

Dr Charlotte Slade, a PhD student at the Institute and clinical immunologist at The Royal Melbourne Hospital, is investigating the genetic changes that cause common variable immune deficiency (CVID), one of the most common forms of primary immune deficiency in Australia. Until now the genetic basis of more than 90 per cent of cases of CVID was not known.

"RESEARCH HAS TAUGHT ME NEW SKILLS IN APPROACHING CHALLENGING CASES"

People with CVID require lifelong antibody treatment to supplement their immune systems, Dr Slade said. "A collaboration with Dr Vanessa Bryant and Professor Phil Hodgkin at the Institute, and Professor Jo Douglass at The Royal Melbourne Hospital has identified CVID patients with changes in a group of related genes," she said.

"These newly discovered mutations – which we think are likely to account for an additional 10 per cent of CVID cases – disrupt a signalling pathway within cells called NFκB signalling, which we know is important for immune function."

For one Melbourne family, the critical discovery of the genetic change causing CVID came just in time. "We discovered the mother and daughter were both carriers of the mutated gene," Dr Slade said.

"More importantly, the daughter was in the last trimester of pregnancy and our discovery allowed us to confirm her diagnosis and start her on antibody treatment to help protect her and her baby.

"We are now one step closer to finding new treatments for the condition, which will be life changing for the one in 10,000 people whose immune system cannot defend their body from infections," Dr Slade said.

Dr Slade said the opportunity to make research discoveries that have a direct impact on patients was very rewarding.

"Research has taught me new skills in approaching challenging cases, compared to how I was trained as a clinician. As clinicians we need quick answers in order to help the patient in front of us, but patience and persistence is required to answer these research questions. Nevertheless, I believe these answers, which come slowly, will lead to great improvements in clinical care for many people in Australia and worldwide in the near future.

"Once I have completed my PhD I would like to continue working as a clinician-scientist. I hope that the relationships I have formed at the Institute and with national and international collaborators during my PhD will lead to great opportunities for ongoing and productive research projects," she said.

Fighting cancer with our immune system

A coordinated system of immune cells protects us from invading microbes, and provides long-lasting immunity to infections. Recently it has been recognised that our immune system also has a role in protecting us from cancer.

PhD student Ms Rebecca Delconte, supervised by Dr Nick Huntington, aims to understand how specific immune cells, known as natural killer (NK) cells, can be unleashed against cancer.

"I HOPE THAT MY RESEARCH INTO IMMUNOTHERAPY WILL ONE DAY HAVE CLINICAL APPLICATIONS"

As lead author in two studies published in 2016 in the journals *Nature Immunology* and *Immunity*, Ms Delconte revealed how NK cell activity is controlled by a cell signalling molecule called interleukin-15.

The research focused on proteins within NK cells that influence how the cells respond to interleukin-15 said Ms Delconte, who was funded by a Leukaemia Foundation of Australia PhD scholarship and received a scholarship top-up from Cancer Therapeutics Australia.

"One of our studies identified a protein that boosts NK cell function in response to interleukin-15, while the other pinpointed a protein 'brake' that stifles NK cell activity," she said. "Amplifying NK cell function and taking off the brake could have the potential to improve these cells' ability to attack cancer cells."

Immunotherapy has been at the forefront of cancer research in the past five years, showing success in effectively treating some incurable cancers such as metastatic melanoma.

"I hope that my research into immunotherapy will one day have clinical applications," Ms Delconte said.

When she completes her PhD, Ms Delconte hopes to broaden her skills in translational cancer research. "During my PhD I have had the opportunity to attend international conferences, and to discuss my interests with my mentors at the Institute. These have helped me to plan my future career directions – in the long run I hope that I can learn new techniques, especially in the area of drug discovery," Ms Delconte said.

In addition to laboratory work, Ms Delconte has used her time at the Institute to discuss her research with school students, donors and other community members. "Being given the opportunity to communicate my research in these forums has really made me think more about the broad applications of my research," she said.

‘Holy grail’ of breast cancer prevention in high-risk women may be in sight

People who carry a faulty *BRCA1* gene are at high risk of developing aggressive breast cancer. Currently many women carrying this gene mutation choose surgical removal of their breast tissue and ovaries to reduce their chance of developing breast and ovarian cancers.

PhD student Ms Emma Nolan, Professor Jane Visvader and Professor Geoff Lindeman discovered that an existing medication could have promise in preventing breast cancer developing in women carrying a faulty *BRCA1* gene.

Using samples of breast tissue donated by women with a mutated copy of the *BRCA1* gene, the team were able to pinpoint the cells that give rise to breast cancer.

> “THIS IS POTENTIALLY A VERY IMPORTANT DISCOVERY FOR WOMEN WHO CARRY A FAULTY *BRCA1* GENE, WHO HAVE FEW OTHER OPTIONS”

Cancer precursor cells in *BRCA1*-mutant breast tissue had many similarities to aggressive forms of breast cancer, said Ms Nolan. “These cells proliferated rapidly, and were susceptible to damage to their DNA – both factors that help them transition towards cancer,” she said. “We were excited to discover that these pre-cancerous cells could be identified by a marker protein called RANK. This was significant as inhibitors of the RANK signalling pathway are already in clinical use to treat osteoporosis and breast cancer that has spread to the bone.”

The team showed that inhibiting RANK switched off cell growth in breast tissue from women with a faulty *BRCA1* gene and curtailed breast cancer development in laboratory models.

Professor Lindeman, who is also a medical oncologist at The Royal Melbourne Hospital and the Peter MacCallum Cancer Centre, said the team hoped that RANK inhibition could be used to delay or prevent breast cancer in women with an inherited *BRCA1* gene mutation.

“This is potentially a very important discovery for women who carry a faulty *BRCA1* gene, who have few other options,” Professor Lindeman said.

“To progress this work, RANK inhibitory drugs would need to be formally tested in clinical trials in this setting as they are not approved for breast cancer prevention. A clinical trial has already begun to investigate this further.”

Ms Nolan was awarded the inaugural Professor Joseph Sambrook PhD Student or Postdoctoral Fellow Award, supported by the National Breast Cancer Foundation, for this research. She has now taken up a postdoctoral position at the Francis Crick Institute, UK, investigating the treatment of metastatic cancers.

Collaborating divisions

ACRF Stem Cells and Cancer, Bioinformatics, Systems Biology and Personalised Medicine

Collaborating organisations

Amgen, kConFab, The Royal Melbourne Hospital, the University of Melbourne, Victorian Comprehensive Cancer Centre Familial Cancer Centre

Funding partners

Amgen, Australian Cancer Research Foundation, Australian National Health and Medical Research Council, Cancer Council Victoria, Cancer Therapeutics Cooperative Research Centre, The Joan Marshall Breast Cancer Research Fund, National Breast Cancer Foundation, The Qualtrough Cancer Research Fund, Victorian Cancer Agency, Victorian Government Operational Infrastructure Support Program

More information

Nolan E *et al*. RANK ligand as a potential target for breast cancer prevention in *BRCA1*-mutation carriers. *Nature Medicine*. 2016 Aug;22(8):933-9

People who carry a faulty *BRCA1* gene are at high risk of developing aggressive breast cancer. PhD student Ms Emma Nolan (centre), Professor Geoff Lindeman (left) and Professor Jane Visvader discovered a potential way to prevent breast cancer in some at-risk women.

2016 GRADUATES

Congratulations to the following students who successfully completed their studies this year

Doctor of Philosophy, the University of Melbourne

Dr Kevin Chow

The role of monocyte derived dendritic cells in the allo-response

Professor Andrew Lew, Dr Yifan Zhan, Dr Robyn Sutherland

Dr Farrah El-Saafin

The molecular and cellular function of TAF8 in the embryonic brain

Associate Professor Tim Thomas, Associate Professor Anne Voss

Dr Michelle Gazdik

Investigation of the export pathway in *Plasmodium* parasites utilising small molecule inhibitors of plasmepsin V

Dr Brad Sleebs, Professor Alan Cowman, Dr Justin Boddey

Dr Reema Jain

Molecular control of thymic epithelial cell homeostasis for sustained thymic function

Dr Daniel Gray, Professor Andreas Strasser

Dr Lily Lee

Investigating potential molecular mechanisms that contribute to triple negative breast cancer

Professor Jane Visvader, Professor Geoff Lindeman

Dr Clara Lin

Merozoite surface protein 1 of *Plasmodium falciparum*: insights into complex formation and function in erythrocyte invasion

Professor Alan Cowman, Dr Peter Czabotar

Dr Edmond Linossi

Investigations of the suppressor of cytokine signalling 5

Dr Sandra Nicholson, Professor Nick Nicola, Dr Andrew Webb

Dr Aaron Lun

Statistical analyses of high-throughput sequencing data to study chromatin structure and organisation

Professor Gordon Smyth, Professor Stephen Nutt

Dr Duong Nhu

Towards the synthesis of rocaglamide congeners as potential inhibitor of the eukaryotic initiation factor eIF4A

Associate Professor Chris Burns, Associate Professor Guillaume Lessene

Dr Michelle Palmieri

Understanding PI3K signalling in colorectal cancer – from function to therapy

Associate Professor Oliver Sieber, Dr Bruno Catimel, Associate Professor Joan Heath

Dr Kathryn Potts

Investigating early haematopoietic specification and platelet forming lineage development in the mouse embryo

Dr Samir Taoudi, Professor Doug Hilton

Dr James Rickard

SHARPIN and RIPK1 are key regulators of cell death and inflammation *in vivo*

Professor John Silke, Professor David Vaux

Dr Natalia Sampaio

Modulatory effects of *Plasmodium falciparum* protein PfEMP1 on the monocyte/macrophage innate immune response to malaria

Professor Louis Schofield, Dr Emily Eriksson

Dr Rebecca Stewart

Characterisation of molecular regulation and intracellular signalling of the *Toxoplasma gondii* lytic cycle

Associate Professor Chris Tonkin, Professor Alan Cowman

Dr Stephanie Tan

Preclinical evaluation of glycosylphosphatidylinositol as a potential multi-stage malaria vaccine

Professor Louis Schofield, Dr Emily Eriksson, Professor Geoffrey McFadden, Dr Ethan Goddard-Borger

Dr Sofonias Tessema

Patterns of antibody acquisition to the major variant surface antigen of *Plasmodium falciparum*

Associate Professor Alyssa Barry, Professor Ivo Mueller, Dr Diana Hansen

Dr Andreea Waltmann

The molecular epidemiology of malaria in Solomon Islands

Professor Ivo Mueller, Associate Professor Alyssa Barry

Master of Philosophy, the University of Melbourne

Mr Bryan Lye

Developing a quantitative framework for immunotherapy

Professor Phil Hodgkin, Dr Susanne Heinzel

Masters of Research, the University of Melbourne

Mr Beinan Wang

Investigating the role of a novel inhibitor of MOZ in B cell development and lymphoma

Associate Professor Tim Thomas, Associate Professor Anne Voss

Mr Haoyu (Bruce) Yang

Discovering novel target genes that are critical for p53 mediated tumour suppression

Professor Andreas Strasser, Dr Marco Herold

Ms Yuan (Laura) Yao

Overcoming therapeutic barriers in multiple myeloma by targetting the pathway to apoptosis

Professor David Huang, Professor Andrew Roberts

Bachelor of Science (Honours), the University of Melbourne

Ms Camille Awburn

Establishing a multiplex-tandem PCR assay for the diagnosis and surveillance of soil-transmitted helminth infections in South East Asia

Dr Aaron Jex, Associate Professor Harin Karunajeewa, Dr Suparat Phuanukoonnon

Ms Kimberly Callaghan

Investigating the roles of tryptophan C-mannosylation in protein folding and function

Dr Ethan Goddard-Borger, Dr Jeff Babon

Ms Li Jin Chan

Characterisation of monoclonal antibodies that modulate the interaction between *Plasmodium vivax* adhesin PvRBP2b with its reticulocyte receptor transferrin receptor 1

Dr Wai-Hong Tham, Dr Jakob Gruszczyk

Mr Nick Chandler

Investigating mechanisms of T cell receptor activation

Dr Melissa Call, Dr Matthew Call

Ms Michelle Clark

Hepatitis B vaccine efficacy in Indigenous Australians

Professor Marc Pellegrini, Dr Greg Ebert

Mr Leon Connor

Identification of dense granule proteins in *Toxoplasma gondii*

Associate Professor Chris Tonkin, Dr Justin Boddey

Mr Anthony Copeland,

Overcoming SMAC-mimetic resistance in acute myeloid leukaemia

Dr Gabriela Brumatti, Professor John Silke

Ms Bethany Davey

The study of essential aspartyl proteases across the malaria parasite lifecycle

Dr Justin Boddey, Professor Alan Cowman

Ms Katherine Davies

Structural and biochemical analysis of activation, oligomerisation and membrane permeabilisation by the mixed lineage kinase domain-like (MLKL) protein

Dr James Murphy, Dr Peter Czabotar, Dr Emma Petrie

Ms Brigette Duckworth

Determining individual T cell fates *in vivo* using a novel multi-colour fluorescent reporter system

Professor Gabrielle Belz, Professor Phil Hodgkin, Dr Susanne Heinzel

Ms Alexandra Gurzau

Understanding the ATPase domain of the epigenetic regulator Smchd1

Dr James Murphy, Associate Professor Marnie Blewitt, Dr Kelan Chen

Ms Cassandra Harapas

Investigating FGFR3-TACC3-driven cancers of the respiratory epithelium

Dr Kate Sutherland, Dr Marie-Liesse Asselin-Labat, Dr Sarah Best

Mr Robert Hennessy

Investigation of murine natural killer cell homeostatic proliferation and survival

Dr Kim Pham, Dr Nicholas Huntington

Mr Miles Horton

Analysis of T cell heterogeneity at the clonal level

Professor Phil Hodgkin, Dr Susanne Heinzel

Ms Rachel Joyce

Investigating the roles of the epigenetic regulator PRC2 and histone modification in mammary gland development and tumourigenesis

Professor Jane Visvader, Dr Ewa Michalak

Ms Ashleigh Kropp

Structural insights into DCLK1 regulation

Dr Isabelle Lucet, Associate Professor Chris Burns

Mr Oliver Le Grice

Comparative quantitative analysis of epigenetic modifiers to identify novel treatments for pathogenic B cells

Dr Edwin Hawkins, Professor Phil Hodgkin

Ms Anna Lieschke

Elucidating the mechanisms underpinning immune senescence

Professor Benjamin Kile, Dr Stephane Chappaz

Ms Tamara Marcus

Generation of an adenoviral reporter system for detection of Wnt and Notch signalling in colon organoids

Dr Nadia Kershaw, Professor Tony Burgess, Dr Maree Faux

Ms Kristy Meiselbach

Prognostic implications of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios in determination of overall and progression-free survival in pancreatic cancer patients

Dr Tracy Putockzi, Associate Professor Peter Gibbs

Ms Rhiannon Morris

Are receptors, JAKs and STATs the only essential mediators of the IL6 signalling pathway?

Professor Doug Hilton, Dr Andrew Jarrett

Mr Tom Peers-Barlow

Determining the therapeutic efficacy of a bifunctional combi-drug in acute myeloid leukaemia

Dr Najoua Lalaoui, Professor John Silke, Associate Professor Chris Burns

Ms Kristin Rigbye

Investigating the transcriptional and translational regulation of mixed lineage kinase domain-like in necroptosis-related disease

Professor John Silke, Dr Joanne Hildebrand, Dr James Murphy

Mr Joel Rimes

Quantitative analysis of JQ-1 as a therapeutic for systemic lupus erythematous

Dr Edwin Hawkins, Dr Susanne Heinzel

Mr Andrew Sealey

Testing CTx-8014, a new class of cancer therapeutic, in an *in vivo* model of hepatocellular carcinoma

Associate Professor Joan Heath, Dr Karen Doggett

Ms Melissa Shi

Deciphering the membrane topology of Bak and Bax apoptotic pores

Dr Ruth Kluck, Dr Rachel Uren

Ms Olivia Stonehouse

Investigating the role of ZFP831 in the haematopoietic system

Dr Samir Taoudi, Dr Shalin Naik

Ms Santini Subramaniam

Efficient enrichment of trace amounts of *Plasmodium vivax* DNA from human blood

Associate Professor Alyssa Barry, Professor Melanie Bahlo

Ms Dana Tabbara

Next-generation mucolytics to treat lung diseases

Dr Ethan Goddard-Borger, Professor Ben Kile

Ms Tania Tan

Global changes in chromatin architecture upon introduction of the transcription factor PAX5

Dr Rhys Allan, Professor Stephen Nutt, Dr Tim Johanson

Mr Christopher Traill

Design and synthesis of novel TBK1 inhibitors for treating rheumatoid arthritis

Associate Professor Chris Burns, Dr Brad Sleebs

Ms Stephanie Tresize

Characterising the differentiation of follicular B cells into antibody secreting cells in *Ppapdc1b-/-*, *Itm2c-/-* and *Clptm1l* del/del mice

Professor Stephen Nutt, Professor Lynn Corcoran

Ms Mary-Louise Wilde

Investigating the role of protein kinase A in *Plasmodium falciparum* infection of red blood cells

Associate Professor Chris Tonkin, Professor Alan Cowman

Ms Athena Williamson

Apoptotic caspases are essential for the suppression of DAMP signalling

Professor Benjamin Kile, Dr Mark van Delft

VISIBLE AND INSPIRING LEADERS

New laboratory heads expand research capabilities

Four new laboratory heads were appointed in 2016, boosting the Institute's research programs in immunology, cancer, computational biology and bioinformatics.

Our new faculty members were:

Dr Melissa Davis, who uses computational biology to study the regulatory networks that control the behaviour of cells in normal and cancerous tissues. One focus of this has been to understand the processes that underpin breast cancer metastasis.

Dr Misty Jenkins, the Institute's Cory Fellow, who is investigating how immune T cells seek and destroy cancerous and virus-infected cells, and how this can be used to enhance cancer immunotherapies.

Dr Wei Shi, who develops computational methods for biological investigations. These have been used to discover genetic changes implicated in immune disorders and cancers, as well as making sense of the genes that impact the function of the immune system.

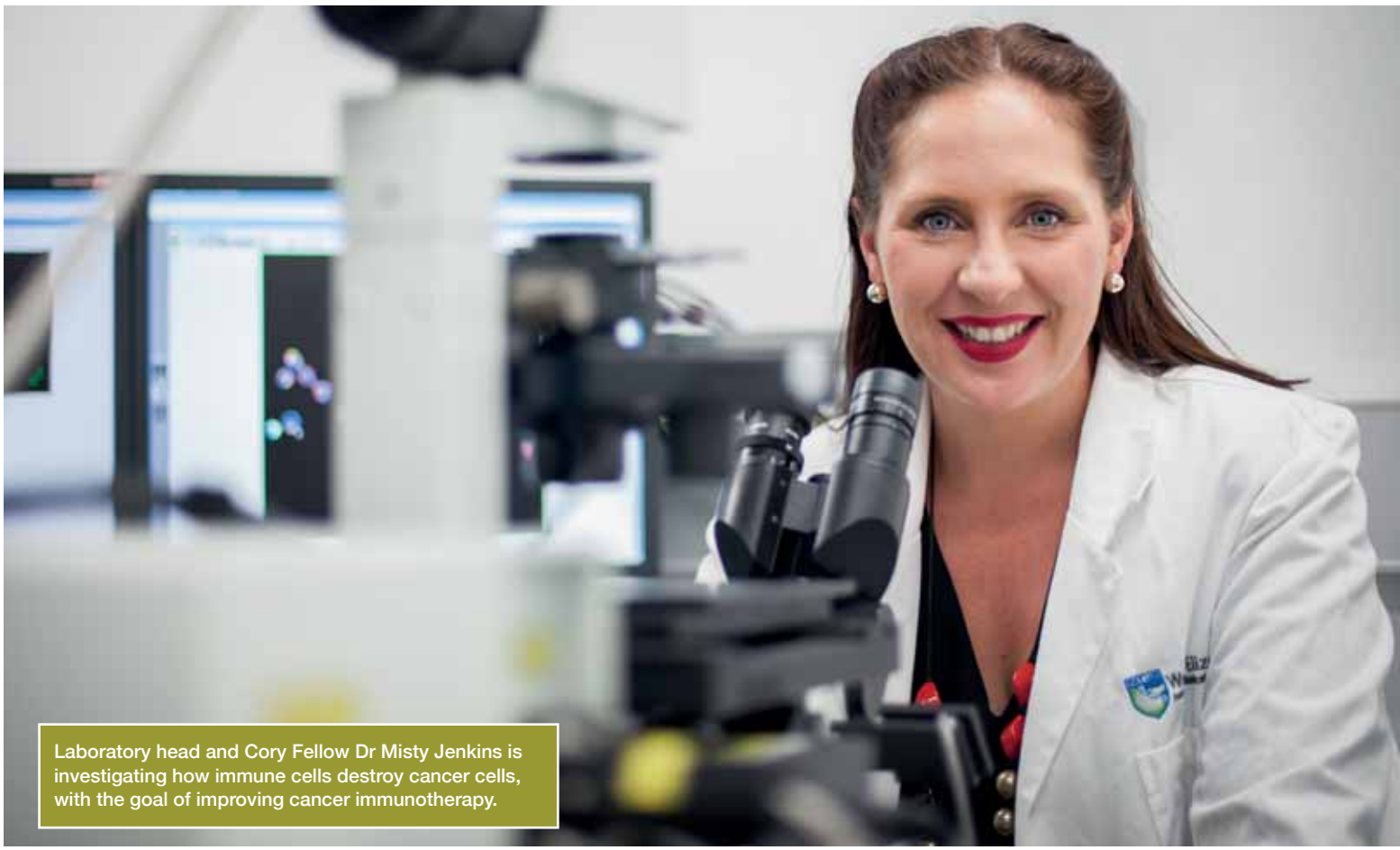
Professor Christine Wells, who uses bioinformatics and genomics to understand how cells develop and become activated. Her research has focused on how immune cells and stem cells interact to repair injured tissue.

Pioneering researchers honoured with election to learned academies

Institute researchers were recognised in 2016 by two national learned academies for their significant contributions to science, outstanding leadership and distinguished professional achievements.

Breast cancer researcher Professor Geoff Lindeman and molecular immunologist Professor Stephen Nutt were among 21 Australian researchers elected to the Australian Academy of Science. Their election brings to more than 15 the number of current Institute scientists who are fellows of the academy.

The Australian Academy of Health and Medical Sciences acknowledged four senior Institute scientists' research contributions in the fields of inflammatory diseases, breast cancer, cell death and haematology. Professor Ian Wicks, Professor Jane Visvader, Professor Andreas Strasser and Professor Benjamin Kile were among the 50 new fellows elected to the academy, a body established to promote health and medical research and its translation to enable a healthier community both in Australia and globally.



Laboratory head and Cory Fellow Dr Misty Jenkins is investigating how immune cells destroy cancer cells, with the goal of improving cancer immunotherapy.

Immunology researcher recognised by Women of Influence Awards

Immunology researcher Dr Misty Jenkins was named in *The Australian Financial Review* and Westpac 100 Women of Influence Awards for 2016.

Dr Jenkins was a finalist in the Innovation category of the awards, in recognition of her contributions to medical research, reconciliation and gender equity.

"I HOPE THIS INSPIRES A NEW GENERATION OF WOMEN TO PURSUE THEIR PASSION"

Dr Jenkins leads a research team investigating the biology of white blood cells called cytotoxic T cells. These cells are the serial killers of the immune system, and their job is to seek and destroy cancerous and virus-infected cells.

A descendant of the Gunditjmara people of Western Victoria, Dr Jenkins is deputy chair of the National Centre of Indigenous Genomics. This body is overseeing the creation of a repository of Indigenous biospecimens, genomic data and documents for research and other uses that benefit Australian Indigenous communities and the general Australian community.

Dr Jenkins said she was thrilled to be recognised by the awards. "These awards honour the often-overlooked contribution to science, business and industry made by women," she said. "I hope this inspires a new generation of women to pursue their passion."

Queen's Birthday award recognises gender equity champion

Institute director Professor Doug Hilton was appointed an Officer of the Order of Australia as part of the 2016 Queen's Birthday Honours List.

The award recognised Professor Hilton's service to medical research, in particular his advocacy for gender equity in science and his commitment to supporting young researchers.

"THE ABILITY TO FOLLOW YOUR CURIOSITY BUT ALSO WORK TO IMPROVE THE HEALTH, ECONOMY AND INNOVATIVE SPIRIT OF THE COUNTRY IS A GREAT PRIVILEGE"

Professor Hilton said he felt humbled by the award. "It has been amazing to work with so many brilliant and passionate people – my mentors, my peers and many younger scientists," he said. "The ability to follow your curiosity but also work to improve the health, economy and innovative spirit of the country is a great privilege."

Professor Hilton's research has spanned from fundamental science to innovative development. His research achievements include discovering hormones and pathways used by cells to communicate with each other. He was also the director of the Cooperative Research Centre for Cellular Growth Factors for five years, co-founded a biotechnology company and spearheaded collaborations with international and Australian biopharmaceutical companies.

Since his appointment as the sixth director of the Institute in 2009, Professor Hilton has championed initiatives to redress gender imbalance at senior levels of medical research. In 2015 he was appointed an inaugural Male Champion of Change by the Victorian Equal Opportunity and Human Rights Commission.

Clinician and PhD student Dr Ruth Mitchell won the inaugural Australian Medical Association Doctor in Training of the Year award for her work in the care of fellow doctors.

Dr Mitchell, who is also a neurosurgical registrar at The Royal Melbourne Hospital, was recognised for her "tireless pursuit of doctors' wellbeing" and "high quality care through advocacy, education and research".

DIVERSITY AND INCLUSION

Diversity is a key driver of innovation. The Institute is working hard to create an environment that enables us to attract and retain the talent we need to drive innovation and excellence with a positive and supportive culture at its core.

Our goal is to ensure our workplace fully reflects the diversity in the Australian community. To achieve this we must build an inclusive organisation and ensure the diverse voices of our people are heard and have influence. We continue to strive to create an environment where all our people have equal access to employment opportunities and we have diversity of representation at senior levels.

Building a holistic approach to diversity and inclusion

In 2016, the Institute completed the development phase for its first diversity and inclusion strategy.

The strategy will embed and extend the gains we have made and take our achievements to the next level through a focus on inclusion, evidence-based decision making, and developing sustainable leadership to ensure diversity and inclusion becomes part of everything we do. The framework will align to the Institute's strategic goals and priorities; support, guide and coordinate our current activities and identify new priorities.

NAB Community Grant to tackle unconscious bias

The Institute was awarded a $50,000 community grant from NAB for the implementation of training to tackle unconscious bias in the workplace.

More than 140 staff undertook the training, which focused on recognising and mitigating the everyday biases that can unconsciously impact judgements, decisions and behaviours and, in turn, organisational policies and processes.

Diversity and inclusion manager Ms Louise Johansson said the initiative supported the Institute's objective of being a leader in diversity and inclusion in the medical research sector.

"Bringing these skills into the workplace will help to effect positive outcomes for all staff including career advancement and a greater representation of women in science," Ms Johansson said.

Diversity is a key driver of innovation at the Institute.

In 2016 a team including (from left) Mr Andrew Giang, Dr Susanne Heinzel, Professor Phil Hodgkin and Professor Lynn Corcoran discovered how the size of an immune response is regulated.

A long-term commitment to reconciliation

The Institute is committed to ensuring that our research makes a meaningful contribution to improving health outcomes for Aboriginal and Torres Strait Islander peoples.

We recognise that to do this our researchers must understand that health and wellbeing are not isolated from wider social, cultural and economic issues in the short or longer term.

5 Aboriginal and Torres Strait Islander interns

4 reconciliation-focused seminars and events

55 Aboriginal and Torres Strait Islander school students visited the Institute

4 events to celebrate Aboriginal and Torres Strait Islander history and culture

3 organisations working to improve Indigenous health and education outcomes supported

Innovation key to second Reconciliation Action Plan

In 2013, the Institute made the decision to join Reconciliation Australia's Reconciliation Action Plan (RAP) program, in recognition of the need to make a formal commitment to reconciliation.

In 2016 our second *Innovate RAP 2016-2018* was launched, which continues to strengthen our ongoing support for reconciliation. This builds on the strong foundation provided by our inaugural *Reflect RAP*.

The key areas of focus in our *Innovate RAP* are:

- **relationships:** solidify existing relationships between the Institute and Aboriginal and Torres Strait Islander stakeholders, and reach out to new partners, to deepen our knowledge, extend our impact and strengthen our science;
- **respect:** involve Aboriginal and Torres Strait Islander peoples at every stage of the Institute's work, by continuing to build an Institute that has respect for Aboriginal and Torres Strait Islander peoples at its core; and
- **opportunities:** nurture the next generation of Aboriginal and Torres Strait Islander leaders through our internship program and replicate this across our entire workforce bringing in the best and brightest scientists, students and professional services staff; open up our supply chain to Aboriginal and Torres Strait Islander owned and run businesses; and support local organisations working to improve outcomes for Aboriginal and Torres Strait Islander peoples.

The development and implementation of the RAP is overseen by the Institute's Reconciliation Committee. Institute director Professor Doug Hilton said Aboriginal and Torres Strait Islander people were central to the development of the *Innovate RAP*.

"We particularly acknowledge the advice, guidance and support from our Aboriginal and Torres Strait Islander committee members Dr Ngaree Blow, Dr Shayne Bellingham, Dr Robert James and Ms Kristy Meiselbach," Professor Hilton said. "We also recognise the expert contribution from our external advisory group made up of Aboriginal and Torres Strait Islander leaders in our local community.

"They have provided us with invaluable insights to understand from their perspective how the Institute can make a difference to the lives of Aboriginal and Torres Strait Islander peoples through our research and other activities," Professor Hilton said.

"…YOU HOLD FUTURE HOPES IN YOUR HANDS. YOUR INNOVATION, YOUR IMAGINATION, YOUR EXPERIMENTATION AND YOUR ILLUMINATION OF THINGS UNSEEN AND THE UNKNOWN… TO CELEBRATE OUR FUTURE WE MUST ACKNOWLEDGE OUR PAST BOTH IN ITS SUCCESS AND ITS FAILING FOR IN BOTH WE CAN FIND UNITY."

– Mr Robert Young
(Gunnai, Gunditjmarra, Yorta Yorta, Wiradjuri)

In celebration of the Institute's *Innovate RAP*, the Institute commissioned a new artwork, 'In Your Hands', by Koorie artist Mr Robert Young (left), pictured with Wurundjeri Elder Aunty Diane Kerr (centre) and Institute director Professor Doug Hilton.

Pilot program to improve representation of women in science

The Science in Australian Gender Equity (SAGE) Athena SWAN pilot is an initiative of the Australian Academy of Science and the Australian Academy of Technology and Engineering. Based on a UK accreditation program, the initiative is designed to spearhead action on gender equity in science, technology, engineering, mathematics and medicine.

The Institute was one of 32 organisations to commence the two-year program in 2016 to work towards obtaining an Athena SWAN Bronze Institutional Award. Successful organisations must demonstrate a solid foundation for eliminating gender bias and developing a culture that is inclusive of gender diversity.

To achieve accreditation, the Institute must exhibit:

- quantitative data, including staff hiring, promotion, retention, return to work and supported productivity post-parental leave;
- qualitative data, including gender equity policies, practices, systems, flexible arrangements and career satisfaction;
- evidence of gender equity challenges and opportunities for improvement;
- a four-year action plan based on data assessment, current policies and lessons learned; and
- implementation of an organisational structure for data collection and self-assessment to follow through on actions identified over the next four years.

In 2016 the Institute's self-assessment team began the process of analysing data and other evidence to understand the barriers to achieving gender equity. A launch event and consultation workshop were held in November to share initial findings and test actions with Institute staff and students.

> "I SEE THE SAGE PILOT AS BEING AN IMPORTANT INITIATIVE THAT BRINGS TOGETHER THE MANY DIVERSE ORGANISATIONS THAT ARE COMMITTED TO GENDER EQUITY"

Institute director Professor Doug Hilton said he was delighted to see the progress of the SAGE Athena SWAN pilot.

"I see the SAGE pilot as being an important initiative that brings together the many diverse organisations that are committed to gender equity," Professor Hilton said. "A sector-wide approach gives us the best chance to succeed, and consequently the best chance for Australian researchers to make the important discoveries our community needs."

In 2016 more than 150 Institute staff signed up to become allies for gender equity as part of the Athena SWAN advocate program. The advocates pledged to promote the Athena SWAN program within their work group, to call out sexist behaviour wherever it occurs, and to support 50:50 gender balance for speakers and panels.

Partnerships emphasise the need for gender equity

The Institute is committed to working collaboratively with other organisations to pursue initiatives that promote gender equity in the scientific sector and Victorian workplaces more widely.

Male Champions of Change Victoria is part of a national initiative bringing together influential men in corporate, government and community leadership positions to tackle gender equity through action and advocacy.

Institute director Professor Doug Hilton is one of the Victorian Male Champions of Change. The Institute, along with other member organisations, has committed to taking action in five key areas: measurement and accountability; personal leadership; everyday sexism; flexible work; and the prevention of violence against women.

CEO Conversation, an initiative of Chief Executive Women, provided the space for open dialogue and shared learning between the director and his senior leadership team about the gender equity challenges facing the Institute. It also gave Institute leaders the chance to share experiences with women who have made it to the top of corporate Australia.

Women in Science Parkville Precinct (WiSPP) is a local initiative involving five medical research institutes in Parkville, aiming to generate a collaborative effort to increase the retention of women in science and the numbers of women in science leadership.

WiSPP undertakes a range of work including learning and development activities such as a cross-sector mentoring program and a metrics project that is designed to measure the impact of collective initiatives to overcome barriers for women in science across the five institutes.

Family violence workplace support policy launched

One in six women and one in twenty men over the age of fifteen have been subject to domestic and family violence. The prevalence of domestic and family violence in Australia means it is an issue that is relevant to all Australian workplaces – including the Institute.

In 2015, Professor Doug Hilton and his fellow Male Champions of Change called on workplace leaders to "play their part" in reducing the prevalence and impact of domestic and family violence.

> "DOMESTIC AND FAMILY VIOLENCE IS AN ISSUE THAT WE CAN ALL TAKE RESPONSIBILITY TO PREVENT OR MITIGATE"

In October 2016 the Institute launched its first family violence workplace support policy, which acknowledges this as a workplace issue, recognises the impact it may have on staff, and offers workplace support and safety to staff experiencing family violence.

Domestic and family violence advocate Ms Kristy McKellar spoke at the launch, sharing her personal story and highlighting the work that is underway to help strengthen family violence policies in Australia.

Professor Hilton said that while it was easy for employers to consider that 'home' and 'family' are separate from 'work', it was important to remember that they all impact employees.

"By ensuring people experiencing domestic and family violence know that they have access to the appropriate support and services we hope to ease – in some small way – the difficulties they experience," Professor Hilton said.

"We also sincerely hope that in the long term the prevalence of family violence in Australia will be reduced by a greater community awareness – including within workplaces – that family violence ultimately impacts all of us in some way. Domestic and family violence is an issue we can all take responsibility to prevent or mitigate."

To show support for the United Nations Women's 'Orange the World' initiative and the 16 Days of Activism against Gender-Based Violence Campaign, the Institute coloured its *Illuminarium* orange from 25 November – the International Day for the Elimination of Violence against Women – to 10 December – Human Rights Day.

Early Childhood Education and Care facility to support Institute parents

The Institute has introduced a range of initiatives to address the gender imbalance at senior levels in the medical research sector. However, access to childcare continues to be identified as a significant obstacle to women's career development.

In late 2015 the Institute's board endorsed a proposal to establish an on-site Early Childhood Education and Care centre at the Institute's Parkville campus. The initiative had been championed by the Institute's Gender Equity in Science Committee over many years, with the first Institute-wide childcare survey undertaken in 1994.

"THE WORKFORCE BENEFITS THAT ON-SITE CHILDCARE WILL BRING WILL ULTIMATELY LEAD TO MORE DISCOVERIES THAT WILL IMPROVE HEALTH OUTCOMES IN AUSTRALIA AND GLOBALLY"

In 2016 the Institute appointed Perkins Architects to design a 100 place, five-level facility. The ground floor will provide office space, a kitchen and a flexible, multipurpose space suitable for combined activities. Other levels have been designed to meet the needs of specific age groups. Services will be open to all Institute families and will include long day care and an Early Learning Centre incorporating three-year-old and four-year-old kindergarten programs.

Construction will commence in 2017 and the new facility will open in early 2018. A service provider to operate the facility will be appointed in mid-2017.

The Early Childhood Education and Care centre has received more than $2 million in philanthropic support, through major donations from Professor Terry Speed and Mrs Sally Speed, and The Dyson Bequest.

The project also received a boost from the Victorian Government, with the awarding of a $650,000 2016-17 New Early Learning Facilities grant. The project has additionally received support from Melbourne Health. The use of air space above existing Melbourne Health carparks has enabled a design that allows all children to have access to outdoor play space on each level.

This initiative is the first of its kind for an Australian medical research institute. The workforce benefits that on-site childcare will bring will ultimately lead to more discoveries that improve health outcomes in Australia and globally.

Planning is underway to establish a new Early Childhood Education and Care centre at the Institute's Parkville campus by 2018.

SECURING THE SUPPORT WE NEED

The Institute does not exist in isolation. To achieve our goals, we rely on productive partnerships with external organisations, and on the support of the community.

In 2016 Melbourne Museum's *Biomedical breakthroughs: a new view of you* exhibition celebrated the scientific achievements of the Institute and our industry partner CSL.

BRINGING THE INSTITUTE AND OUR COMMUNITY TOGETHER

The Institute exists to benefit our local, national and global community through advancing healthcare, and we depend on our community for support. Our public events program provides unique opportunities to engage with our community, raising awareness of the mission and achievements of the Institute and the broader Australian research sector.

More than 4800 people attended events and activities hosted by the Institute in 2016. Our diverse program of events and activities reached a broad range of people including healthcare consumers, research supporters, prospective students, Institute alumni, collaborators and government representatives, including many people who had not previously heard of the Institute.

Silver Screen Science

In partnership with the Melbourne Writers Festival, the Institute hosted its second Silver Screen Science film festival in August. More than 500 film buffs and science lovers gathered at the Australian Centre for the Moving Image (ACMI) for special screenings of three science-themed films: *Never Let Me Go, I Am Legend* and *Jabbed – Love, Fear and Vaccines*. These were followed by opportunities for audience questions, and illuminating discussions between expert panels of Institute scientists and Melbourne storytellers.

Art of Science exhibition

The Atrium at Federation Square was transformed for 10 days in August with a pop-up art exhibition showcasing the 15 finalists in the Institute's annual Art of Science awards. More than 1300 people, young and old, were mesmerised by the stunning images captured by Institute researchers.

Open House Melbourne

In July, the Institute opened its doors as part of Open House Melbourne, welcoming more than 500 visitors over one weekend. Guided tour groups had the opportunity to see the laboratories where some of the world's most exciting research is underway, and to meet and ask questions of more than 60 staff and students who volunteered for the event.

Discovering our research

More than 1550 people took part in Institute discovery tours in 2016. Guests including school and university students, community groups, international clinicians, and others with an interest in medical science were taken behind the scenes of our laboratories. Visitors regularly commented on how much they enjoyed their chance to see the Institute's state-of-the-art equipment, hear about the latest medical research and meet our world-class scientists.

A new book, *Let there be light: 100 years of discovery at the Walter and Eliza Hall Institute*, was launched at the Institute's 2016 Annual General Meeting. From left: Institute director Professor Doug Hilton, Melbourne University Publishing editor Ms Cathy Smith, author Ms Anne Crawford, the Institute's head of Communications and Marketing Ms Penny Fannin and board president Mr Christopher Thomas.

Century of medical breakthroughs celebrated at Melbourne Museum

The history and achievements of Victorian medical research were showcased in a Melbourne Museum exhibition that brought the inner workings of the human body to life through interactive and immersive experiences.

The *Biomedical breakthroughs: a new view of you* exhibition, produced by the museum in partnership with the Institute and Melbourne-based biopharmaceutical company CSL, celebrated the centenaries of the Institute (founded in 1915) and CSL (founded in 1916), and featured historic items from both organisations.

"THE EXHIBITION WAS A FANTASTIC WAY FOR OUR COMMUNITY TO LEARN ABOUT THE WORLD-LEADING MEDICAL RESEARCH THAT OCCURS IN OUR STATE"

Institute director Professor Doug Hilton said the five-month exhibition provided many examples of how the Institute and CSL had improved health in Australia and worldwide.

"Many Victorians aren't aware of the numerous advances in healthcare we take for granted today that originated in medical research laboratories right here," he said. "The exhibition was a fantastic way for our community to discover the world-leading medical research that occurs in our state."

The exhibition highlighted the close ties the Institute has had with CSL since the two organisations were established.

"In the 1920s and 1930s the first antivenoms for Australian snakes were developed through collaborations between Institute and CSL researchers," Professor Hilton said.

"Today we continue to work closely on a range of translational research. The Institute's bioinformatics and immunology researchers are also the beneficiaries of generous support from CSL to our centenary campaign."

A centrepiece of the exhibition was an immersive dome projecting animations of biological processes created by Walter and Eliza Hall Institute biomedical animator Dr Drew Berry.

Dr Berry said in the past century our understanding of human biology had moved from what we could largely see with the naked eye or a weak microscope down to the atomic scale.

"It's just vast and mind-boggling what we are discovering about how our bodies work," he said. "We can't see the molecules that are keeping us alive and controlling our health, so with our animations we aim to represent what scientists – including those right here in Melbourne – are discovering about the inner workings of our own bodies."

The *Biomedical breakthroughs: a new view of you* exhibition at Melbourne Museum used interactive and immersive experiences to showcase the achievements of the Institute and our industry partner CSL.

Strengthening links with Institute alumni

The achievements of the Institute's 101-year history have been the result of the endeavours of thousands of dedicated staff and students.

Institute alumni can be found throughout the world working in diverse roles, and many alumni remain in contact with each other, or with the Institute, both at the professional and the social level.

The Institute's 2015 centenary celebrations afforded many opportunities to reconnect with our alumni. Many stories and memories were shared, and these were collated into a new *Alumni Recollections* book, edited by Dr Emanuela Handman and Professor Jim Goding, both alumni themselves.

> "WITH SUCH A PROUD CULTURE OF COLLABORATION AND MENTORSHIP, IT IS NO SURPRISE THAT I OFTEN MEET ALUMNI WHO REMEMBER THEIR TIME AT THE INSTITUTE WITH FONDNESS AND GRATITUDE"

Our alumni make many contributions to Institute life. During 2016, many alumni presented scientific seminars, offered mentorship to students or attended Institute events.

Institute director Professor Doug Hilton said the Institute's alumni were a community of many diverse and talented people. "With such a proud culture of collaboration and mentorship, it is no surprise that I often meet alumni who remember their time at the Institute with fondness and gratitude," he said. "When I reflect on the achievements of our alumni – who include in their ranks research leaders, renowned educators, dedicated clinicians, and inspiring entrepreneurs – I am proud to think that everyone who has contributed to the Institute has been impacted by our values."

To continue to strengthen the Institute's ties with its alumni, an alumni relations manager was recruited in 2016, ensuring these important and valued relationships are maintained.

Recognising the global network of Institute alumni, an inaugural overseas alumni reunion was held in New York, US. Institute alumnus and event host Associate Professor Paul Cooper said the reunion brought together 16 alumni who had been at the Institute at different times, and were now working in a range of fields in the eastern United States. "We had a wonderful time getting to know each other, sharing stories and warm reflections," he said. "There was a consensus among the alumni that the Institute was a special and unique place to work and the highly collaborative culture and values made it unique in the world."

New events and other opportunities to reconnect with alumni are planned for 2017. We welcome all alumni to join us, email **alumni@wehi.edu.au** to stay in touch.

Institute alumni were among the guests at the launch of the Institute's Art of Science exhibition at Federation Square.

Animation shines light on benefits of vitamin D

The latest scientific understanding of how the sun influences our genetic code was highlighted in 2016 by a new WEHI.TV animation, *Sunshine Vitamin*.

Award-winning biomedical animator Dr Drew Berry said the animation explained how vitamin D is activated by the sun, and 'switches on' processes such as the making of proteins that strengthen our bones.

> "WE WERE PORTRAYING MOLECULES IN THE BODY WHICH, BEING SMALLER THAN THE WAVELENGTH OF LIGHT, ARE IMPOSSIBLE TO FILM AND DIFFICULT TO IMAGINE"

"*Sunshine Vitamin*, along with the other striking biomedical animations produced through WEHI.TV, gives people an intuitive understanding of the remarkable activity occurring in the body's cells and tissues," Dr Berry said.

"In this case we were portraying molecules in the body which, being smaller than the wavelength of light, are impossible to film and difficult to imagine.

"The animation is part of a series designed to explain complex scientific processes easily to a broad audience."

Working as a biomedical animator for more than 20 years at the Institute, Dr Berry has dedicated his career to explaining biological discoveries in a way that is engaging and easy to understand.

"As a trained cell biologist, I'm fluent in the language of science. With my animations, I act as an interpreter for medical research, and as an artist I'm constantly inspired by incredible discoveries," Dr Berry said.

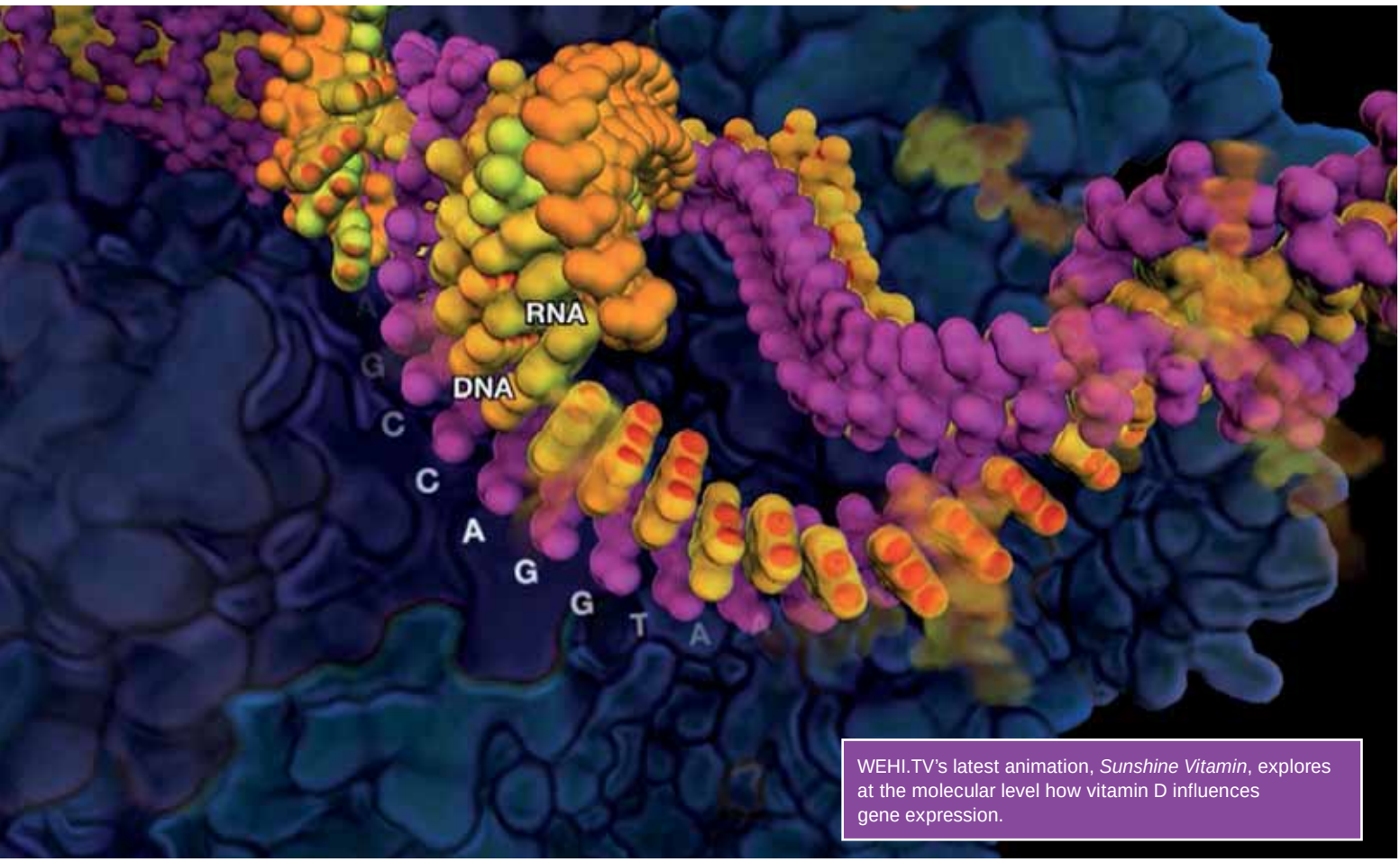
"WEHI.TV is about sharing what is happening at the frontier of medical research in an accurate and entertaining way."

Employing visual tricks from cinema, Dr Berry carefully builds his animations.

"I use colour to pull people through the narrative and to evoke feeling: 'healthy' is usually a palette of pinks and reds because as mammals we associate warm tones with being alive," he said.

Dr Berry said there was a strong demand in the community for meaningful information – especially around complex scientific topics and where health issues are concerned.

"WEHI.TV animations work extremely well as a communication tool for science as they are like a powerful microscope into the body, allowing people to appreciate at the most intricate level what we are all made of," Dr Berry said.



WEHI.TV's latest animation, *Sunshine Vitamin*, explores at the molecular level how vitamin D influences gene expression.

Donors catalyse discoveries

In 2016, about one-quarter of vital funding for the Institute was generously provided from philanthropic sources, including donations, grants, gifts in wills and interest earned on endowed funds.

Perhaps more importantly, philanthropic gifts and grants empowered the Institute to be bold in its research ideas, to support promising young scientists, and to invest in essential technology. It is these investments in people, ideas and technology that we believe will ultimately lead to the next discoveries.

However, this also involves taking risks.

It is our individual supporters who have been willing to support an innovative idea with seed funding, back a young scientist through the challenging early years or purchase a new piece of equipment that will provide astonishing insights into medical biology.

We hope that this year's annual report conveys the important role of donors in our research. We really could not do it without you.

In 2016 we received more than 1400 gifts and grants from hundreds of generous donors, all of whom shared our passionate commitment to making discoveries that both advance our knowledge of major diseases, and improve treatment of these diseases. In total, donors contributed more than $18.736 million to the Institute's research, an increase of 15 per cent on the 2015 result.

"WHEN WE WORK TOGETHER, GREAT DISCOVERIES ARE MADE AND PATIENTS' LIVES ARE TRANSFORMED"

In addition, by the end of 2016 we had 17 Centenary Fellowship donors who have pledged almost $20 million to 19 early-career researchers. Given the challenging landscape of government funding, these fellowships are transformative for younger researchers who can now confidently plan their research over a five-year timeframe. This provides them with the support and certainty they need while they establish the track records that will secure government grants.

There are a number of unique elements that have contributed to the Institute's success over the past 100 years. Collaboration – within research teams, across divisions and with colleagues nationally and internationally – is certainly a defining quality of the Institute, which has proved to be the only way to deliver the major discoveries that transform global health care.

Equally as impactful is the long-term involvement of our generous supporters, who often share this journey with us for many decades and ensure that as an Institute we can remain committed to tackling the significant and complex health challenges facing humanity. This is a journey of peaks and troughs – sometimes experiments fail, sometimes funding falls short – but when we work together, great discoveries are made and patients' lives are transformed.

There is much to celebrate in 2017. Thank you for your continuing support.

Multiple sclerosis is a debilitating chronic neurological condition with no known cause. The Walter and Eliza Hall Trust Centenary Fellowship, funded by the Institute's founding benefactor, is supporting Dr Simon Willis' investigations of the triggers for multiple sclerosis.

OUR SUPPORTERS

The supporters who make our discoveries possible

The advances in medical science at the Walter and Eliza Hall Institute are made possible by our generous supporters. We are proud to acknowledge these gifts, grants and bequests received from 1 January to 31 December 2016. Gifts of $1000 or more are acknowledged, unless otherwise requested by our donors.

The Institute acknowledges the support of the Australian Government through funding from schemes including the National Health and Medical Research Council and the Australian Research Council, and from the Victorian Government through schemes including the Operational Infrastructure Support Program.

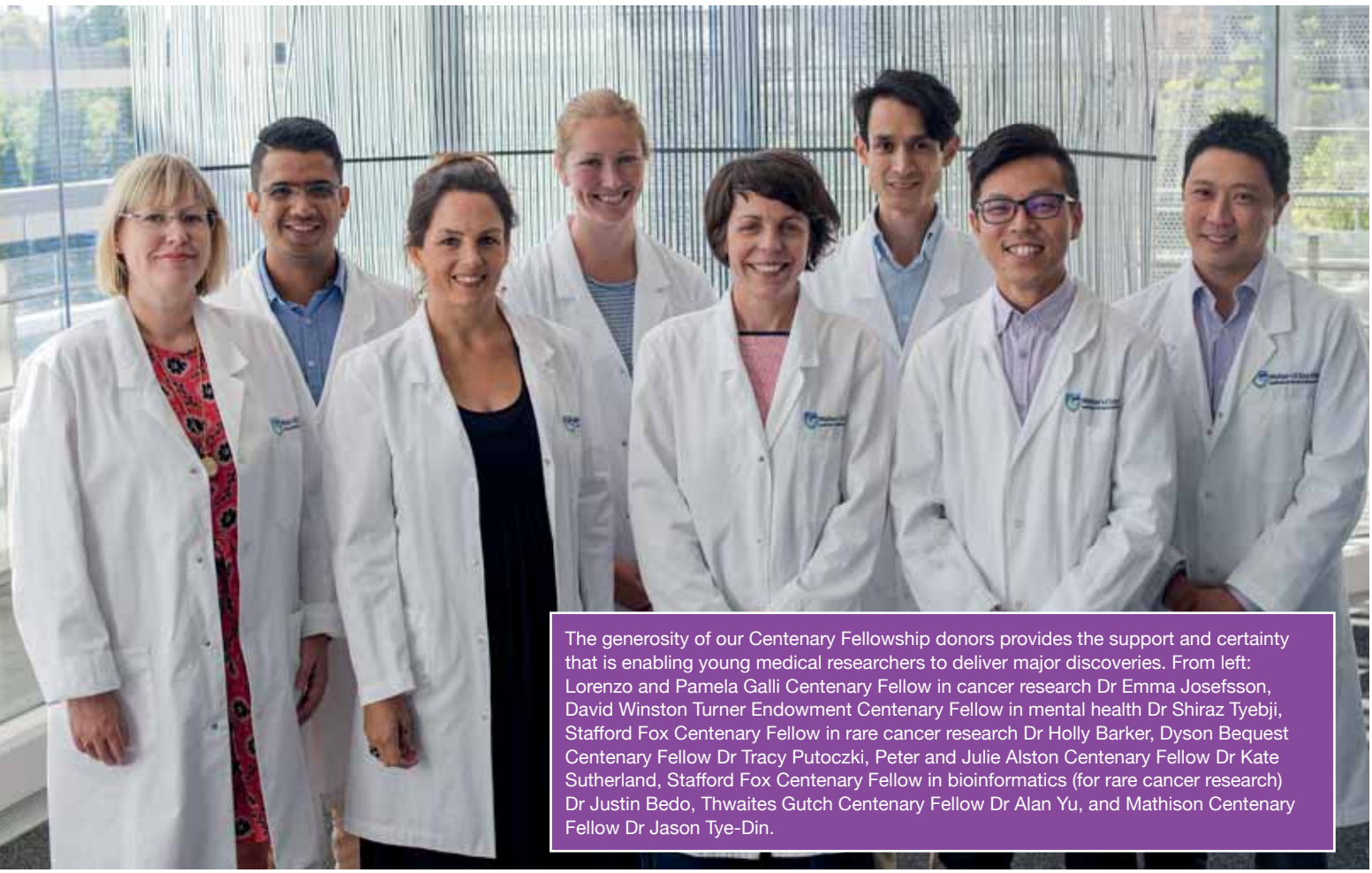
Centenary donors

Founding Centenary donors

Mr Malcolm Broomhead
CSL Ltd
L.E.W. Carty Charitable Fund
The Dyson Bequest
The Alfred Felton Bequest
The Stafford Fox Medical Research Foundation
The Walter & Eliza Hall Trust
Mrs Jane Hemstritch
Ormond College co-funding The Thwaites Gutch Endowment
The University of Melbourne (Mathison Fellows)

Leadership Centenary donors

Estate of Julie Florence Alston
DHB Foundation
Lorenzo and Pamela Galli Charitable Trust
The Metcalf Family
John T Reid Charitable Trusts
David Winston Turner Endowment Fund



The generosity of our Centenary Fellowship donors provides the support and certainty that is enabling young medical researchers to deliver major discoveries. From left: Lorenzo and Pamela Galli Centenary Fellow in cancer research Dr Emma Josefsson, David Winston Turner Endowment Centenary Fellow in mental health Dr Shiraz Tyebji, Stafford Fox Centenary Fellow in rare cancer research Dr Holly Barker, Dyson Bequest Centenary Fellow Dr Tracy Putoczki, Peter and Julie Alston Centenary Fellow Dr Kate Sutherland, Stafford Fox Centenary Fellow in bioinformatics (for rare cancer research) Dr Justin Bedo, Thwaites Gutch Centenary Fellow Dr Alan Yu, and Mathison Centenary Fellow Dr Jason Tye-Din.

International grants

Grants of more than $500,000

Leukemia & Lymphoma Society, US
Ludwig Cancer Research, US
Bill & Melinda Gates Foundation, US

Grants of up to $500,000

Worldwide Cancer Research (Formerly AICR), UK
Global Health Innovative Technology Fund, Japan
Wellcome Trust, UK
Harry J. Lloyd Charitable Trust, US
Howard Hughes Medical Institute, US
Multiple Myeloma Research Foundation, US

Grants of up to $100,000

Foundation for Innovative New Diagnostics, Switzerland
Cancer Research Institute, US
PATH Malaria Vaccine Initiative, US
Coeliac UK
Juvenile Diabetes Research Foundation, US
The Lustgarten Foundation, US

Individual and family philanthropy

Transformational Gift

Anonymous (1)
Professor Terry Speed and F E (Sally) Speed

Gifts up to $200,000

Anonymous (2)
The Joan Marshall Breast Cancer Research Fund
Mr Colin North OAM and Dr Susan Alberti AC
Mr Edward Vellacott and Mrs Morna Vellacott

Gifts up to $50,000

Anonymous (1)
Beck Family Foundation
Mrs Yvonne Butterfield
Ms Sue Clifton
Brian M Davis Charitable Foundation
Mr Michael Fitzpatrick and Ms Helen Sykes
The Isabel & John Gilbertson Charitable Trust
Mr Michael Harris and Ms Kelli Garrison
Dr George James
Mrs Avis Macphee AM and Dr Alex Macphee
Ms Marie McDonald
Professor Jacques Miller AC
Mr Shane Murphy
Mrs Sam Sharman
In memory of Marcel Smits
Mrs Margery Snowball
Ms Pauline Speedy (passed away July 2016)

Gifts up to $10,000

Anonymous (4)
The Shirley Cuff Cancer Research Foundation
Mrs Andrea Gowers and Mr Geoff Gowers
Mr Bob Munro
Nossal Family Trust
The Barbara Luree Parker Foundation Ltd
Craig Perkins Cancer Research Foundation
Ms Caroline Richardson
RobMeree Foundation
Mrs Jean Williamson

Gifts up to $5000

Anonymous (8)
6A Foundation
Mr Angelo Bladeni
Dr Peter Czabotar
Mr John Edward Davies
Demak Timber and Hardware
Professor Richard Divall (passed away Jan 2017)
Mr Graham Gilpin
Professor David Huang
H & K Johnston Family Foundation
Mrs Caroline Johnston
Ms Helen Kennan
Associate Professor Guillaume Lessene
Mr Roger Lines
Mr Brian Little
Dr Darren Lockie
Mr Brendan Madigan
Mrs Christine McConnell and Mr Denis McConnell
Mrs Joyce O'Brien
Professor David Penington AC
Miss Heather Phiddian
Professor Andrew Roberts
Mrs Margaret Ross AM
Mrs Barbara Ruse and Mr Peter Ruse, Mr Adrian Ruse, Mr Christopher Ruse, Ms Nona Ruse
Mr Keith Satterley
Mrs Penny Stott
Ms Jenny Tatchell
Mrs Jean Thomas and Mr Ralph Thomas
Mr Duncan Tuck
Ms Heather White
Mr David Williamson

Gifts up to $2000

Anonymous (9)
Dr Peter Adams and Dr Sheryl Lawson
Australian Society of Cytology
The Joan Elaine Barry Memorial Fund
Con and Trish Boekel and Family
Dr Margaret Brumby AM and Mr Ian Brumby
Mrs June Clapton
Mrs Helen Cochrane and Mr Bruce Cochrane
Associate Professor John Collins and Mrs Mandy Collins
Mrs Mayda Devlin
Mr Mark Devlin and Mrs Elizabeth Devlin
Dr Janice Dudley
Ms Susan Easton-Bond
The Dina & Ron Goldschlager Family Charitable Foundation
Goodman Foundation
Mrs Suzanne Gow
Mrs Margaret Hayes
Ms Meaghan Heritage
Mr Trevor Hilton
Mr Matthew Hilton
Mrs Ann Hilton-Ley
Mr Graham Jackson and Mrs Barbara Jackson
Mrs Margaret Johnson
Mr Donald Kay and Mrs Caryl Kay
Mr Maurice Kelly and Mrs Mary Kelly
Mrs Margot Kilcullen and Mr Rob Kilcullen
Mr George Kiossoglou and Ms Glenda Kiossoglou
Mr John McRae
Mrs Ann Naylor
Mr Cyril Evans and Mrs Pauline Evans
Mr Dieter Rinke and Mrs Maxine Rinke
Mrs Kay Szonert
Mrs Olive Thurlby
Mr Robert Vance and Mrs Claire Vance
Mr John Walker QC and Mrs Angela Walker

Community groups

Australian Rotary Health
Berwick Opportunity Shop
Bonegilla Old Time Dances
Coeliac Australia
Coolah Lady Golfers
Rotary Club of Eltham
Rotary Club of Point Gellibrand
Strathmore Community Services Ltd
Tarneit Skies Resident Association Inc
The Victoria Golf Club Ltd
Twin Towns Services Community Foundation Limited
Yarra Yarra Golf Club

Community fundraisers

Ms Melissa Bowyer
Ms Bev Bradford
Ms Sadie Carr
Ms Sandra Gatt
Ms Lisa Seymour
YLC Vic for Type 1 Diabetes research

Companies and institutions

AMP Foundation
BHP Billiton Matched Giving Program
Donald Cant Watts Corke
National Australia Bank
Corporate Responsibility

Gifts in wills

(listed by bequest amount)

Anonymous (2)
Estate of Gerald Addison Brook Riley
Estate of Vivienne Paul
Estate Pamela J Barclay
Estate of Marlene Anne Brown
Albert H Maggs Charitable Trust
Estate of Valma Clare Burton
Estate of Alan G L Shaw
Estate Dorothy Mary Braund
Estate of Sheila Mary Helpman
Estate of Maxwell Gardiner Helpman
Estate of Jack Ainsworth Rider
Irene & Ronald MacDonald Foundation
The Jakob Frenkiel Charitable Trust
Estate of Diane Adrienne Lemaire
Estate of Eleanor Margrethe Albiston
(The Stang Bequest)
Frederick and Winifred Grassick
Memorial Fund
The Hazel & Pip Appel Fund
Estate of Harold Thomas Swanton
Estate of Ethel Mary Drummond
Estate of Joan Elizabeth Wright
Estate of Beryl Hazel Sparks
Estate L Magrath-Cusworth
Estate of Joan Louise McMahen
Estate of Patricia Ann Gowdie
Estate of Yvonne Agnes Aitken Morgan
Estate of Mary Claire Kemp
Estate of Emily Vera Winder
The C.H. Boden Memorial Trust
Agnes Maude Reilly Charitable Trust
Estate of Florence Lillian Rosier
Estate John Kelvin Julian
John Frederick Bransden Charitable Trust
The Baldy Trust Fund
GT & L Potter Charitable Trust
Margaret Lewis Reilly Charitable Trust
The Frank Broadhurst Memorial
Charitable Fund
Estate of the late Doreen Merle Taylor

Grants

(listed by grant amount)

Anonymous (2)
National Breast Cancer Foundation
The Viertel Charitable Foundation
Leukaemia Foundation of Australia
Cass Foundation Ltd
Cancer Council Victoria
DHB Foundation
Motor Neurone Disease Research
Institute of Australia
The Jack Brockhoff Foundation
Coeliac Australia
The Snowdome Foundation
The Phyllis Connor Memorial Trust
FSHD Global Research Foundation
The Ian Potter Foundation
The Harry Secomb Foundation
JDRF Australia
The Thomas William Francis
& Violet Coles Trust
The Scobie and Claire Mackinnon Trust
Diabetes Australia
Therapeutic Innovation Australia
Bethlehem Griffiths Research Foundation
Joe White Bequest
Cure Brain Cancer
Shepherd Foundation
Drakensberg Trust
The Clive and Vera Ramaciotti Foundation
The Hermon Slade Foundation
Harold & Cora Brennen Benevolent Trust
Kidney Health Australia
Harold and Pam Holmes Charitable Trust
Janko-Inge Foundation
The Medical Advances Without
Animals Trust (MAWA)
Telematics Course Development Fund
Rebecca L Cooper Medical
Research Foundation
Royal Australasian College of Physicians
The Angior Family Foundation
Lung Foundation Australia
Brain Foundation
MS Research Australia
Bionomics
Amelia Eliza Holland Trust
Cancer Council New South Wales
Bell Charitable Fund
Collier Charitable Fund
Haemophilia Foundation Australia
The HMA Foundation
The Lettisier Foundation
Ovarian Cancer Australia
Alan Gordon McMillen Charitable Endowment
Cure Cancer Australia Foundation
The William Angliss (Victoria) Charitable Fund
The Pierce Armstrong Foundation
Australian & New Zealand Head
and Neck Cancer Society
The Eirene Lucas Foundation
Nell & Hermon Slade Trust
The Australia & Pacific Science Foundation
State Trustees Australia Foundation – Rupert,
Ethel & Ronald Fraser & Ruby Thomas
The J Elliston Endowment

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National Australia Trustees
Perpetual Trustees
State Trustees

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Founding Gifts

Mr Chris Thomas and Mrs Cheryl Thomas
CSL Limited
Professor David Gearing and
Mrs Julie Gearing

Leadership Gifts in 2016

Anonymous (2)
Associate Professor Paul Cooper
Urquhart Charitable Fund

Tribute Gifts in 2016

Anonymous (2)
Mrs Barbara Anderson
Mr W R Brookman
Ms Sue Clifton
Dr Ann Cornish
Professor Suzanne Cory ac and
Professor Jerry Adams
Dr Simon de Burgh
Professor David de Kretser ac
Ms Daniela Di Cara
Ms Roz Edmond
Dr Jennifer Favaloro
Ms Diane Gugger
Mrs Geraldine Handasyde
Mr Michael Jeffs
Mrs Margaret Johnson
Mater Haematology Department
Ms Joan Matison
Mr Bill Matthewson and
Mrs Elizabeth Matthewson
Mrs Elizabeth Mottram
Dr Karen Murphy
Miss Ella Noorian
Mr Ray Pederick and Mrs Patricia Pederick
Mr David Russell and Mrs Dianne Russell
Mr Thomas Russell and Mrs Patricia Russell
Professor E. Richard Stanley and
Professor Pamela Stanley
Dr Arthur Tatnall and Mrs Barbara Tatnall
Mrs Jean Thomas and Mr Ralph Thomas
Mrs Jenny Yeats

MEMBERS OF THE INSTITUTE to 31 December 2016

The Royal Melbourne Hospital
The University of Melbourne
Dr Susan Alberti AC
Professor Emeritus Robin Anders
Professor James Angus AO
Mr Donald Argus AC
Mr Barry Axtens
Mr Paul Barnett
Ms Helen Barry
Mrs Ann Bates
Mr Robert Bates
Mr Lance Bauer
Chairman, The Walter and Eliza Hall Trust
Dr Elsmaree Baxter
Professor Glenn Begley
Professor Claude Bernard
Mr Marc Besen AC
Dr Gytha Betheras AM
Associate Professor Rufus Black
Dr Peter Brennan
Mr Malcolm Broomhead
Professor Graham Brown AM
Mrs Rosalind Brown
Mrs Beverley Brownstein
Dr Gerard Brownstein
Mr Ian Brumby
Mr John Brumby AO
Dr Margaret Brumby AM
Professor Tony Burgess AC
Professor Christopher Burrell AO
Professor Robert Burton
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Mr Terry Campbell AO
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Mr Stephen Daley
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Professor Ashley Dunn
Mr John Dyson
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Mr Michael Fitzpatrick
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Professor Richard Fox
Mrs Nolene Fraser
Mr Paul Fraser
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Professor David Gearing
Mrs Julie Gearing
Mrs Janet Gilbertson
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Mrs Jean Hadges
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Mr Murray Jeffs
Mr Jose Jimenez
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Mr Rowan Kennedy
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Mrs Rowena MacKean OAM
Mrs Avis Macphee AM
Ms Eve Mahlab AO
Mrs Robyn Male
Mr Roger Male
Mrs Lorrie Mandel
Ms Nerissa Mapes
Mr Barrie Marshall
Mr John Marshall
Ms Josephine Marshall
Professor Emeritus Jack Martin AO
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Mr Erich Mayer AM
Mrs Netta McArthur
Dr Neville McCarthy AO
Professor James McCluskey
Professor John McKenzie AM
Professor Frederick Mendelsohn AO
Mrs Johanna Metcalf
Mrs Josephine Metcalf
Ms Kate Metcalf
Ms Mary Ann Metcalf
Professor Jacques Miller AC
Professor John Mills AO
Mr Robert Minter
Trustee, The Walter and Eliza Hall Trust
Professor Christina Mitchell
Dr Graham Mitchell AO
Dr Judith Mitchell
Mr Barry Moore
Mr Terry Moran AC
Mrs Barbara Morgan
Mr Hugh Morgan AC
Dr George Morstyn
Mr Bob Munro
Mr Tony Murphy
Ms Linda Nicholls AO
Dr Leslie Norins
Mrs Rainey Norins
Mr Colin North OAM
Lady Lyn Nossal
Mr Tom O'Brien AM
Ms Maureen O'Keefe
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Professor Roger Pepperell
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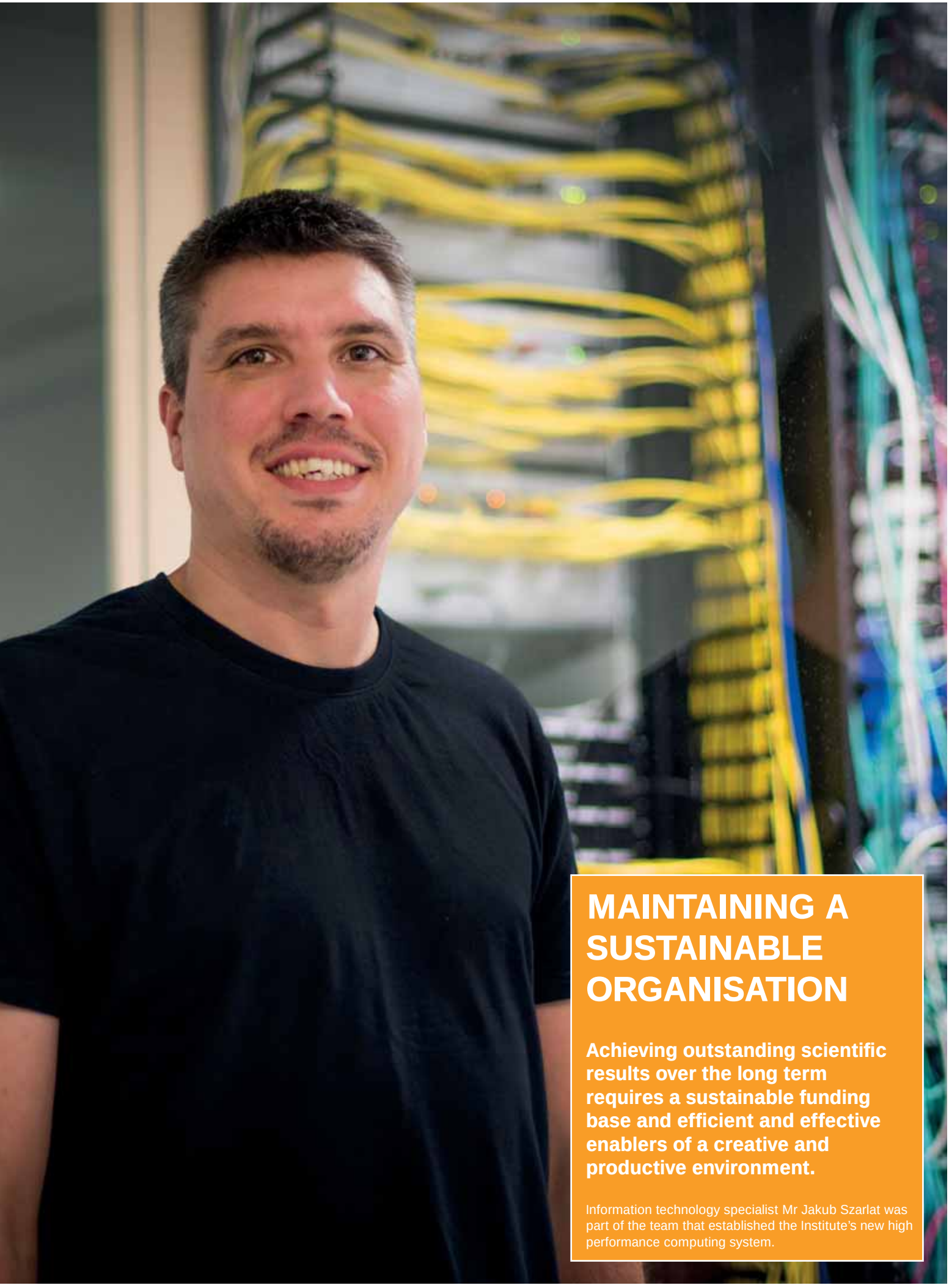
Mr Bruce Teele
Mrs Cheryl Thomas
Mr Chris Thomas AM
Mr John Walker QC
Mr Stanley Wallis AC
Ms Catherine Walter AM
Mr John Walter
Mr John Warburton
Mr Robert Warren
Mrs Catherine Watt
Ms Marion Webster OAM
Mr Kevin Weight
Professor Richard Wettenhall
Dr Senga Whittingham
Mr David Williamson
Mr Malcolm Williamson
Professor Robert Williamson AO
Professor Ingrid Winship
Mr Peter Worcester
Mr Robert Wylie

The Institute remembers those members who have passed away since 2016

Dr David Campbell
Professor Gordon Clunie
Dr Margaret Holmes
Ms Pauline Speedy



MAINTAINING A SUSTAINABLE ORGANISATION

Achieving outstanding scientific results over the long term requires a sustainable funding base and efficient and effective enablers of a creative and productive environment.

Information technology specialist Mr Jakub Szarlat was part of the team that established the Institute's new high performance computing system.

OPERATIONAL OVERVIEW

The Institute's staff and students have participated in a range of activities throughout the year to continue to build a scientific organisation that achieves excellent research outcomes and is a great place to work.

Highlights include greater collaboration opportunities between our scientific and professional services teams, enhancing our capability in high performance computing, and improvements to our scientific service capacity.

These advances, in combination with our inaugural Culture Survey outcomes, will assist us to promote the growth of our great people, great culture and great science into 2017.

New deputy directors appointed

In 2016, the Institute implemented a new management and committee structure to provide a broader platform of leadership, guide our future direction and encourage greater consultation.

"THE INSTITUTE IMPLEMENTED A NEW MANAGEMENT AND COMMITTEE STRUCTURE TO PROVIDE A BROADER PLATFORM OF LEADERSHIP, GUIDE OUR FUTURE DIRECTION AND ENCOURAGE GREATER CONSULTATION"

The restructuring of the deputy director roles has afforded the requisite support for the Institute's director and boosted collaboration opportunities between our scientific and professional services teams, as well as ensuring transparent processes and decision-making.

The Institute's director, Professor Doug Hilton, is now supported by:

- **Professor Alan Cowman, Deputy Director, Scientific Strategy,** further strengthening our commitment to collaborative research and our continuing ability to deliver great science;
- **Ms Samantha Ludolf, Deputy Director, Strategy and Operations,** continuing to lead our professional services team with a focus on building even stronger links between professional services and scientific teams; and
- **Professor David Vaux, Deputy Director, Science Integrity and Ethics,** shaping our policies and practice in this area.

To support our new management structure, changes to the Institute's internal committee structure have also been implemented.

Institute Deputy Director, Strategy and Operations
Ms Samantha Ludolf

Enhancing research infrastructure

Computational biology applies mathematics, statistics and computer science to make sense of biomedical data and biological systems. The Institute's planned growth in computational biology was boosted in 2016 by the launch of a new high performance computing system, including a new research computing cloud.

This new research infrastructure allows scientists to process data at speeds that were previously unthinkable, enhancing the Institute's capabilities in diverse fields including genomics, proteomics and systems biology. Work continues to ensure that our high performance computing system will meet the rapidly changing requirements of research into the future, and growth is maintained in a sustainable manner.

Another strategic focus of 2016 was to ensure the Institute's research imaging infrastructure and management capabilities keep pace in this rapidly developing field. The *2016-2020 Centre for Dynamic Imaging Strategic Plan* was completed (see page 44), guiding investment in infrastructure, technology and people to position the Institute as a world leader in imaging.

Building for the future

Two important infrastructure initiatives in 2016 were the completion of our Kew campus redevelopment, and the progression of our plans for a new Early Childhood Education and Care centre.

The redevelopment of the Clive and Vera Ramaciotti Laboratories was an important aspect of our campus consolidation program that commenced in 2015. The strict quarantine requirements of our bioservices facilities had posed a significant challenge for renovating the Kew campus, meaning that only essential building work had been undertaken since the facility's opening in 1973.

In 2016 we were able to achieve much-needed upgrades and modernisation to the facility's IT, electrical and research infrastructure, as well as improvements in amenities for its dedicated and highly skilled staff. The building works coincided with the relocation of bioservices personnel from our Bundoora campus. It was pleasing to see the realisation of significant cost savings by the broader campus consolidation project in 2016.

Great advances were also made to an important new initiative, our Early Childhood Education and Care centre. From 2018 more than 100 children will be offered care in a new building at our Parkville campus. The centre is an important investment in our workforce, and is a direct outcome of ongoing consultations with staff about how we can enhance diversity and gender equity at the Institute. You can read more about the progress of this landmark project on page 76.

Maintaining a great culture

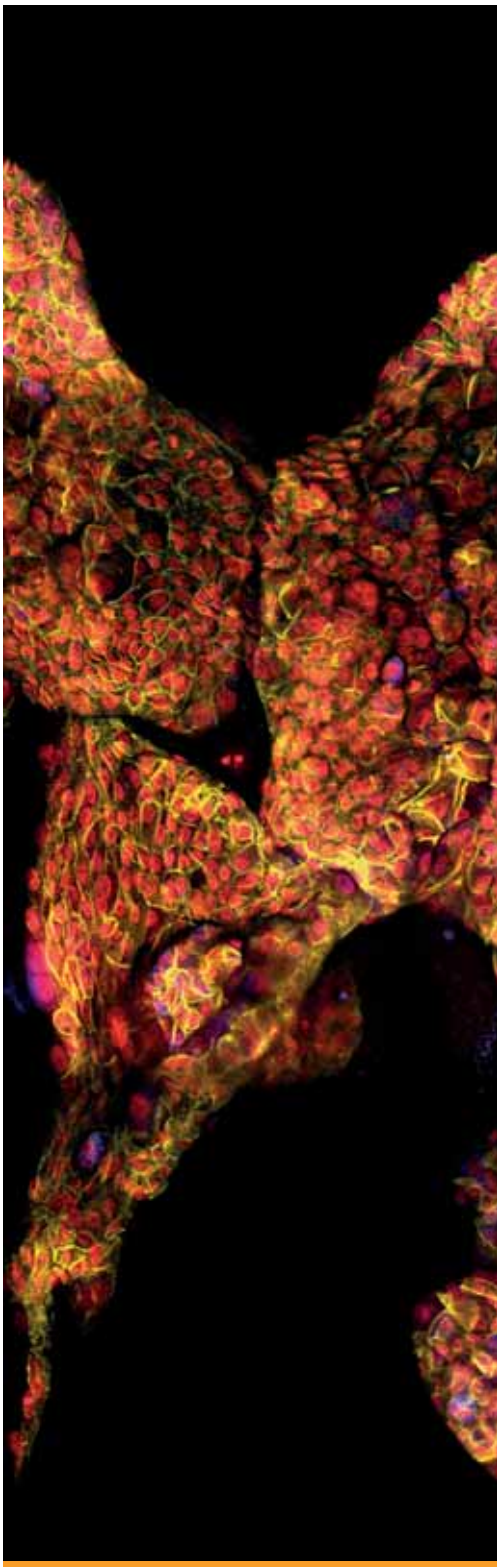
For the Institute to continue to achieve its strategic goal of doing great science, it relies on great people and a great culture. An important focus of our *Strategic Plan 2015-2020* is to ensure that the Institute continues to be a great place to work for everyone.

> "FOR THE INSTITUTE TO CONTINUE TO ACHIEVE ITS STRATEGIC GOAL OF DOING GREAT SCIENCE, IT RELIES ON GREAT PEOPLE AND A GREAT CULTURE"

In 2016 we delivered the Institute's inaugural Culture Survey, to discover and document our staff and students' perceptions of our workplace. It was pleasing that more than 75 per cent of staff and students participated, providing an important baseline measurement of our workplace culture. Their feedback is being used to implement improvements to our working environment, with the goal of enhancing our workplace culture into the future.

Information gathered by our Culture Survey is also invaluable to the progress of key diversity and inclusion initiatives, including our application for an Athena SWAN Bronze Institutional Award through the Science in Australia Gender Equity pilot (page 74), and our development of the Institute's first Diversity and Inclusion Strategy (page 72).

Ms Samantha Ludolf
Deputy Director, Strategy and Operations
Walter and Eliza Hall Institute



Research imaging provides scientists with unique and valuable insights into the three-dimensional structure of biological tissues. This image, captured by lung cancer researcher Ms Clare Weeden, reveals in intricate detail the cells that line structures in the lung called alveoli, which allow the exchange of gases between the blood and the air.

Our *2016-2020 Centre for Dynamic Imaging Strategic Plan* ensures the Institute will continue to be a leader in research imaging into the future.

Vale Dr Margaret Holmes (1921-2016)

It was with great sadness that the Institute community farewelled Dr Margaret Holmes, a loyal alumna and friend of the Institute, who passed away on 28 November 2016.

Margaret was closely associated with the Walter and Eliza Hall Institute for almost 80 years, first as an employee and, since her retirement, a mentor for staff as well as a wonderful friend for many.

"IT WAS MARGARET'S DEDICATION TO EXACTING STANDARDS THAT SET UP THE SYSTEMS THAT CONTINUE TO ENSURE THE INSTITUTE'S RESEARCH IS ALWAYS CONDUCTED AT THE HIGHEST LEVEL"

In 1938 Margaret joined the Institute as a school leaver, one of only 12 staff. In a male-dominated academic world, Margaret had the talent and tenacity to pursue a scientific education while she worked. She later earned a PhD and a scholarship to undertake research in Europe.

She was recruited back to the Institute in 1958 by then director Sir Frank Macfarlane Burnet, where she remained until her retirement in 1986. In this period she oversaw the expansion of staff and infrastructure that underpinned a golden era of discovery at the Institute. Margaret was also an important scientific contributor to many landmark research achievements in understanding the causes and treatment of autoimmune conditions.

Margaret's expertise in animal husbandry was particularly notable, and she oversaw the establishment of the Clive and Vera Ramaciotti Laboratories in 1970, a pioneering facility that continues today. Becoming the Institute's general manager in the late 1970s, Margaret was an integral contributor to the design and development of our new Parkville building that was opened in 1985 and is still in use today.

In 1986 and at the age of 65 – then the age of compulsory retirement – Margaret left the Institute as a staff member, but remained a friend for the next three decades.

Institute director Professor Doug Hilton said Margaret was a pioneer for the women who followed her in biomedical science in Australia, and made many important contributions to the field. "It was Margaret's dedication to exacting standards that set up the systems that continue to ensure the Institute's research is always conducted at the highest level," he said.

"On a personal note, I am among many with wonderful memories of Margaret, who was feisty and indomitable. She was ferocious in her vigilance, and fearless in her commitment to all those in her care," Professor Hilton said.

In honour of Margaret's leadership and talents, the Institute now awards an annual Margaret Holmes Emerging Leader prize, recognising a younger staff member who has made significant contributions to the Institute, and has demonstrated the potential for leadership and continuing service.

Alumni, staff and students gathered in June 2016 to celebrate the birthdays of Institute patron and former director Sir Gustav Nossal (left) and former general manager Dr Margaret Holmes, who sadly passed away in November 2016.

WALTER AND ELIZA HALL INSTITUTE BOARD

The directors of the Walter and Eliza Hall Institute of Medical Research board 31 December 2016

Mr Christopher W Thomas AM

BCom (Hons) MBA *Melbourne* FAICD

Appointed: February 2001
Appointed President: 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 is currently a member of the National Gallery of Victoria's Remuneration and Nomination Committee. 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.

Mrs Jane Hemstritch

BSc (Hons) *London University* FICAEW FICAA FAICD

Appointed: October 2013
Appointed Vice President: July 2016

Mrs Hemstritch was managing director Asia Pacific for Accenture Limited from 2004 until her retirement in February 2007. In this role, Mrs Hemstritch was a member of Accenture's global executive leadership team and oversaw the management of Accenture's business portfolio in Asia Pacific.

She holds a Bachelor of Science with honours in biochemistry and physiology and has professional expertise in technology, communications, change management and accounting.

Mrs Hemstritch is a member of the Council of the National Library of Australia, the Global Council of Herbert Smith Freehills, the Council of Governing Members of The Smith Family and Chief Executive Women. She is an independent non-executive director of Telstra Corporation Ltd, Lend Lease Corporation Limited, Tabcorp Holdings Ltd, and Victorian Opera Company Ltd (chairman from February 2013).

Mr Robert Wylie

FCA FAICD

Appointed: April 2014
Appointed Honorary Treasurer: April 2014

Mr Wylie is a fellow of the Australian Institute of Company Directors, a fellow and past president of the Institute of Chartered Accountants in Australia and a member of the Institute of Chartered Accountants in Scotland. He is a non-executive director of Maxitrans Industries Limited.

Mr Wylie joined Deloitte in 1973 in the United Kingdom, transferring to Australia in 1976. He was national chairman of Deloitte Australia from 1993 to 2001. He was deputy managing partner Asia Pacific from 2001 before joining Deloitte & Touche USA as a senior executive partner from 2002 to 2006. He was also a member of The Deloitte Global Board and Global Governance Committee as well as The Deloitte Consulting Global Board.

Associate Professor Rufus Black

BA LLB (Hons) *Melbourne* MPhil DPhil *Oxon*

Appointed: August 2013

Associate Professor Black has extensive private, public and social sectors experience at both management and governance levels with a deep academic background in ethics.

He is master of Ormond College, president of Museum Victoria, deputy chancellor of Victoria University, a director of the law firm Corrs Chambers Westgarth, and a principal fellow in Philosophy and principal fellow in the Department of Management and Marketing at the University of Melbourne. He teaches in the University of Melbourne's Master of Entrepreneurship degree. He is also chair of the Teach for Australia Board and a director emeritus of the New York-based Teach for All.

Associate Professor Black has previously worked as a partner at McKinsey & Company and has made many contributions to public policy. He holds degrees in law and politics from the University of Melbourne and graduate degrees in moral theology from the University of Oxford, where he was a Rhodes Scholar.

Mr Malcolm Broomhead

BE (Civil) MBA *UQ* FIE FAusIMM FAIM MICE FAICD

Appointed: July 2014

Mr Broomhead is a professional non-executive director. His directorships include BHP Billiton Limited and Orica Limited (chairman).

Mr Broomhead was formerly managing director and CEO of Orica Limited from 2001 until September 2005. Prior to Orica, he was managing director and CEO of the global diversified resources company North Limited.

Mr Broomhead has had extensive experience in the resources industry, as well as in finance, investment and construction activities. He has worked in management positions with Halcrow (UK), MIM Holdings, Peko Wallsend and Industrial Equity.

Mr John Dyson

BSc *Monash* Grad Dip Fin Inv SIA MBA *RMIT*

Appointed: May 2016

Mr Dyson has been an active participant in the venture capital industry for two decades. He is one of the founders of Starfish Ventures, a venture capital company established in Melbourne in 2001, and is chair of Swinburne Ventures Pty Ltd, the entity responsible for the commercialisation of technology for Swinburne University of Technology.

From 1997 to 2002 he was a director of the Australian Venture Capital Association Limited, including deputy chairman in 1998 and chairman in 1999. He is currently a director of technology companies Atmail, Audinate, Myriax, and Space-Time Research. Before moving into venture capital Mr Dyson worked in the investment banking and stockbroking industries for Schroders, Nomura Securities, KPMG and ANZ McCaughan.

Mr Dyson is a passionate alpine skier and is a former chairman of the Mount Buller and Mount Stirling Alpine Resort Management Board, which oversees the management of Victoria's largest alpine resort. He is a co-trustee of the Dyson Bequest, a $15 million charitable foundation that provides grants to a range of social welfare, education and environmental causes.

Professor Jim McCluskey

BMedSc MB BS MD *UWA* FRACP FRCPA

Appointed: April 2011

Professor McCluskey is deputy vice-chancellor (research) at the University of Melbourne and a Redmond Barry Distinguished Professor in Microbiology and Immunology.

He has published more than 310 papers on the genetic control of specific immunity. He established the South Australian node of the Australian Bone Marrow Donor Registry and has consulted for the Australian Red Cross in the area of transplantation matching for more than 25 years.

He is a member of the board of directors of the Bionics Institute, Australian Friends of Asha Slums and UoM Commercial. He is chair of Nossal Institute Ltd. He has previously been a director of the Florey Institute of Neuroscience and Mental Health, St Vincent's Institute and the Burnet Institute. He led the development of the Peter Doherty Institute for Infection and Immunity, a joint venture between The University of Melbourne and Melbourne Health. Most recently, he has been instrumental in leading the multi-institutional team that developed the Atlantic Fellows Social Equity Program supported by The Atlantic Philanthropies.

Ms Marie McDonald

BSc (Hons) LLB (Hons) *Melbourne*

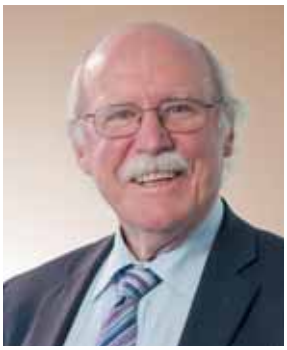
Appointed: October 2016

Ms McDonald was a partner of Blake Dawson (now global law firm Ashurst) from 1990 to 2014. She specialised in corporate and commercial law and, in particular, cross-border mergers and acquisitions and corporate governance.

She was a member of the Australian Takeovers Panel (2001-10) and chair of the Corporations Committee of the Business Law Section of the Law Council of Australia (2012-13) and a deputy chair (2010-11).

Prior to becoming a lawyer, Ms McDonald completed a Bachelor of Science (Honours) degree with first class honours, majoring in chemistry.

Ms McDonald is a non-executive director of CSL Limited and Nanosonics Limited.



Dr Graham Mitchell AO

RDA BVSc *Sydney* FACVSc PhD *Melbourne*
FTSE FAA

Appointed: July 2007

Dr Mitchell completed his PhD at the Walter and Eliza Hall Institute in the late 1960s that involved the discovery of T and B cells.

In 1973, after postdoctoral experience in the United States, United Kingdom and Switzerland, Dr Mitchell returned to the Institute and established a program on the immunology of parasitism. He was also a previous director of research in the R&D Division of CSL Limited.

Dr Mitchell is an adviser on science and innovation to the Victorian Government and is a principal of Foursight Associates. He is a non-executive director of Antisense Therapeutics Limited and Avipep Pty Ltd and has a detailed knowledge of the academia-industry interface and global health.

Mr Terry Moran AC

BA (Hons) *LaTrobe*

Appointed: November 2013

Mr Moran is the former secretary of the Department of Prime Minister and Cabinet and former secretary of the Victorian Department of Premier and Cabinet.

Mr Moran's involvement in the public service has resulted in the establishment of institutions that have made important contributions to Australia's cultural and educational landscape, such as the Wheeler Centre, the Grattan Institute, Opera Victoria, the Melbourne Recital Centre, the Australian and New Zealand School of Government and the National Institute of Public Policy.

He is the board chair for both the Barangaroo Delivery Authority and Melbourne Theatre Company, chair of the Centre for Policy Development and holds the position of senior adviser at the Boston Consulting Group.

Ms Carolyn Viney

LLB/BA *Monash*

Appointed: December 2016

Ms Viney has more than 20 years' experience in construction, property development and real estate investment.

Ms Viney is currently executive general manager development at Vicinity Centres. Over a 13-year period she held a number of senior roles at Grocon, including CEO, deputy CEO, head of development and in-house counsel. Before this, she was a senior associate at law firm Minter Ellison.

Ms Viney is a division councillor of the Property Council of Australia's Victoria division, an advisory board member to the Victorian Government's Office of Projects Victoria and an advisory board member of Women's Property Initiatives, a not-for-profit housing provider to women and children at risk of homelessness.

Professor Ingrid M Winship

MB ChB MD *Cape Town* FRACP FACD

Appointed: June 2007

Professor 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 before combining an academic position at the university with a clinical position.

In 1994, Professor Winship took up an academic position at the University of Auckland where she later became Professor of Clinical Genetics, clinical director of the Northern Regional Genetic Service and associate dean for research in the Faculty of Medicine and Health Sciences (1999-2003). She is currently a member of the Australian Health Ethics Committee and the Victorian Cancer Agency Reference Group. She is on the Executive Management Committee of the Melbourne Genomic Health Alliance and the council of the Peter Doherty Institute.

The following directors of the Walter and Eliza Hall Institute of Medical Research board retired during 2016

Mr Steven Skala AO

BA LLB (Hons) *Qld* BCL *Oxon*

Appointed: June 1999
Appointed Vice President: March 2004
Retired: May 2016

Mr Skala is vice chairman Australia of Deutsche Bank and a former senior partner of Arnold Bloch Leibler. He is also chairman of Blue Chilli Technology Pty Ltd. Active beyond banking and commerce, Mr Skala is chairman of the Heide Museum of Modern Art, deputy chairman of The General Sir John Monash Foundation, a director of the Centre for Independent Studies and is a member of the International Council of New York's Museum of Modern Art. Mr Skala is a former chairman of Film Australia Limited, the Australian Centre for Contemporary Art, Wilson HTM Investment Group Limited, Hexima Limited and The King Island Company Limited. He recently retired from the board of the Australian Broadcasting Corporation where he served as a director for 10 years.

Mr Michael C Fitzpatrick

BA (Hons) *Oxon* BEng (Hons) *UWA*

Appointed: February 2001
Retired: April 2016

Mr Fitzpatrick is chairman of Pacific Current Group and a director of Infrastructure Capital Group. He is a former director of Rio Tinto plc and was chairman of the Australian Football League until April 2017. As the founder and former managing director of Hastings Funds Management Limited, 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.

Dr Gareth Goodier

MB ChB *Sheffield* MHA *NSW* DHSc *Anglian Ruskin Universty* FRACMA FAFPHM

Appointed: August 2012
Retired: October 2016

Dr Goodier is a public health physician who has served as the chief executive of several major health systems and academic hospitals over the past 28 years. Most recently he was appointed as the inaugural executive chair of the Melbourne Biomedical Precinct in November 2016.

Dr Goodier's leadership of academic hospitals includes Melbourne Health, Cambridge University Hospitals, Royal Brompton and Harefield Hospitals, Royal Perth Hospital and the Women's and Children's Hospitals in Perth.
Dr Goodier has also worked as the regional director or CEO of health systems in regional Australia (the Kimberley and North Queensland) and the NHS (North West London Strategic Health Authority) and as a management consultant for Arthur Andersen and the World Bank.

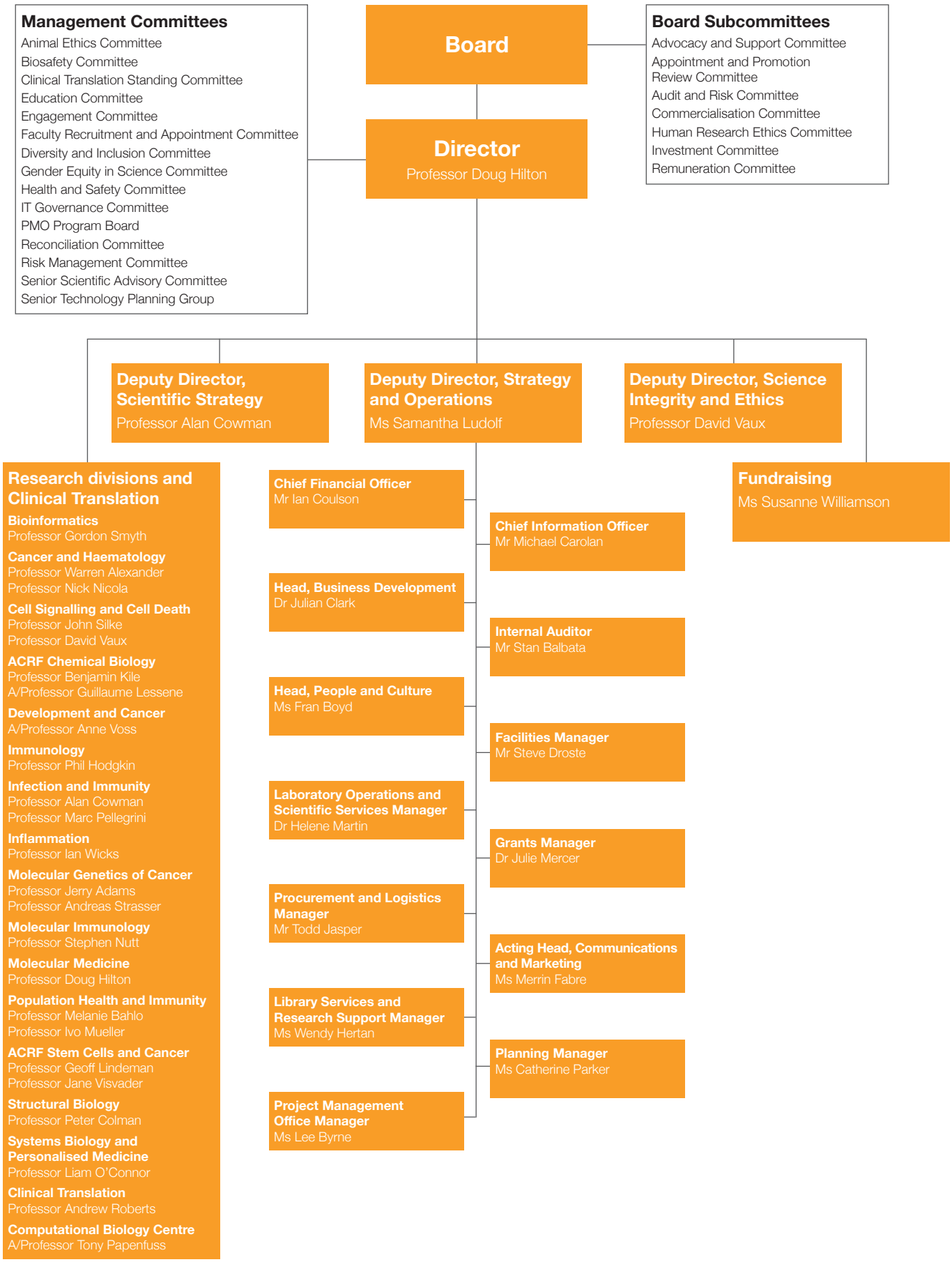
Ms Catherine M Walter AM

LLB (Hons) LLM MBA *Melbourne* FAICD

Appointed: February 2001
Retired: April 2016

Ms Walter is deputy chair of Victorian Funds Management Corporation, a non-executive director of Australian Foundation Investment Company, the Reserve Bank's Payment Systems Board and is chair of Melbourne Genomic Health Alliance. 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.

INSTITUTE ORGANISATION 31 December 2016



The Walter and Eliza Hall Institute acknowledges the support of these organisations

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The Atlantic Philanthropies

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Bill & Melinda Gates Foundation

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Cancer Council Victoria

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Coeliac Victoria and Tasmania

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Cure Brain Cancer Foundation

Cure Cancer Australia Foundation

diabetes australia

Donald Cant Watts Corke

Felton Bequest 1904

FIND Because diagnosis matters

FSHD Global Research Foundation Ltd

Gandel Philanthropy

GHIT Fund Global Health Innovative Technology Fund

The Ian Potter Foundation

JDRF Improving Lives. Curing Type 1 Diabetes.

Leukaemia Foundation Vision to Cure Mission to Care

Leukemia & Lymphoma Society fighting blood cancers

Ludwig Cancer Research

Lung Foundation Australia "When you can't breathe...nothing else matters"

Multiple Myeloma Research Foundation

National Breast Cancer Foundation Funding Research for Prevention and Cure

mvi PATH Malaria Vaccine Initiative

Ramaciotti Supporting Biomedical Research

Rotary International

snowdome Foundation

Therapeutic Innovation Australia

veski

In kind support was received from these organisations

Deloitte.

EgonZehnder

pwc

Harry M. Hearn AM Solicitor

JBWere

SPP

The Walter and Eliza Hall Institute is associated with the following organisations

The Royal Melbourne Hospital

The University of Melbourne

agrf

Athena SWAN Member

Biomedical Research Victoria

Biogrid Australia

Cancer Therapeutics CRC

Cancer Trials Australia

CareerTrackers Indigenous Internship Program

CART-WHEEL

CATALYST therapeutics

GTAC Gene Technology Access Centre

The HEARing CRC

Male Champions of Change Victoria

MRCF

Melbourne Genomics Health Alliance

Museums Victoria

Ormond College

Type 1 Diabetes TrialNet

SupplyNation Member

Victorian Breast Cancer Research Consortium Inc

Victorian Cancer Biobank

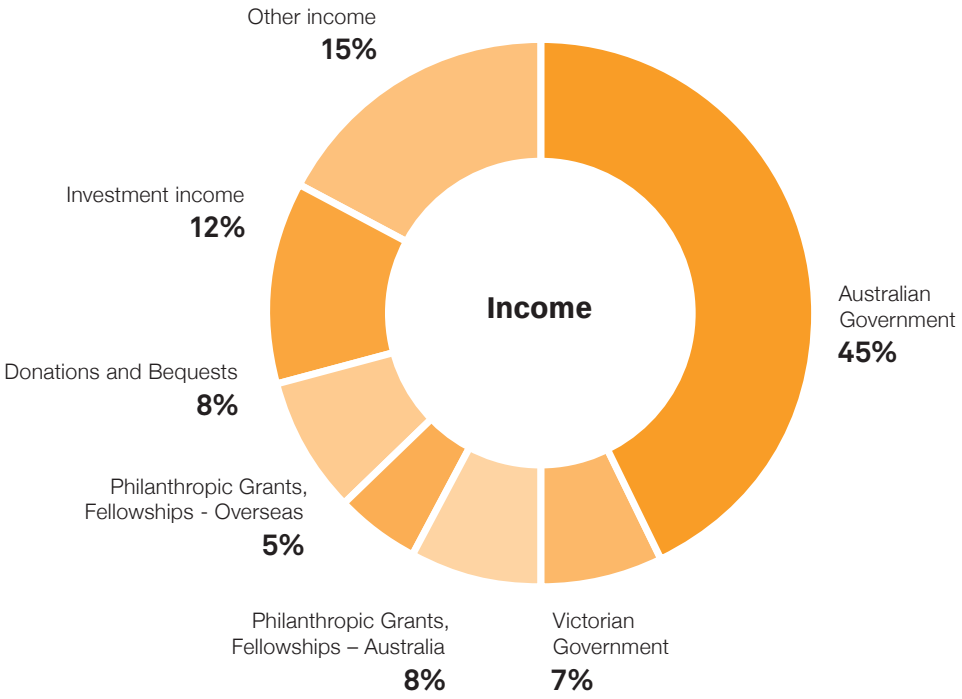
Victorian Comprehensive Cancer Centre

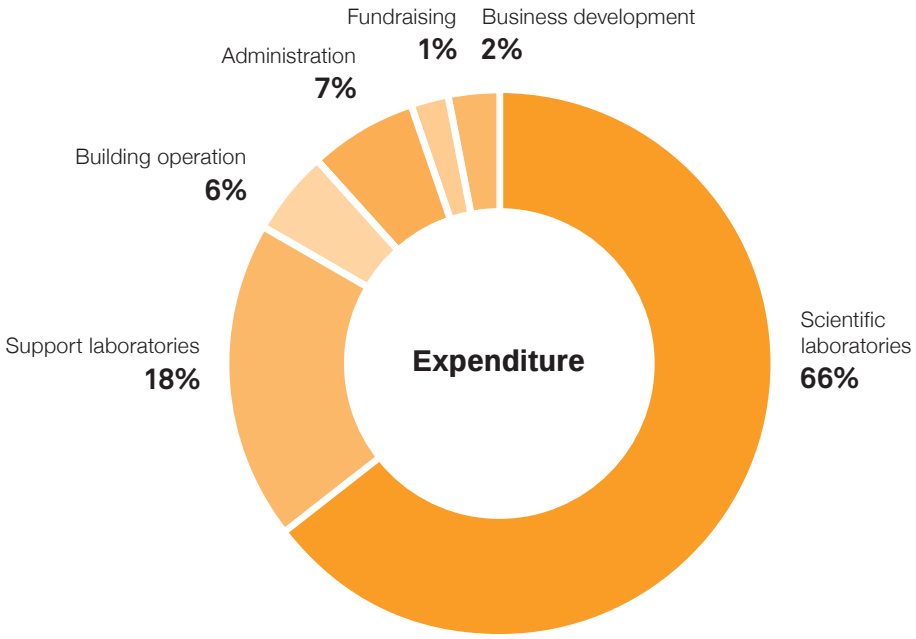
Statistical summary for the year ended 31 December 2016

	2016	2015	6 months to 31 December 2014	12 months to 30 June 2014	2013
	$'000s	$'000s	$'000s	$'000s	$'000s
Research revenue					
Australian Government	51,079	48,492	25,569	51,512	52,995
Victorian Government	7,753	7,419	3,078	6,936	6,771
Foreign governments	1	495	47	506	472
Government revenue	**58,833**	**56,406**	**28,694**	**58,954**	**60,238**
Industrial grants and contracts	3,227	4,691	1,058	1,696	1,482
Philanthropic grants and fellowships – Australia	8,804	8,062	4,659	9,024	6,971
Philanthropic grants and fellowships – international	5,805	7,386	4,056	6,355	5,376
Investment income	13,463	13,172	7,074	12,925	13,146
Royalty income	9,268	2,262	4,727	3,119	828
General revenue	5,746	4,430	1,077	3,369	2,819
Donations and bequests	8,816	7,297	4,126	6,678	4,402
Non-government revenue	**55,129**	**47,300**	**26,777**	**43,166**	**35,024**
Total revenue for research	**113,962**	**103,706**	**55,471**	**102,120**	**95,262**
Research expenditure					
Staff costs	80,652	76,570	38,544	75,027	69,339
Laboratory operating costs	19,025	18,406	9,326	17,841	17,650
Laboratory equipment	3,610	2,285	1,105	2,538	3,487
Building operations	4,673	4,712	2,424	5,171	5,307
Administration	2,198	2,421	1,451	1,985	1,162
Fundraising	387	219	106	-	-
Business development	747	825	390	849	815
Doubtful debts expense	(115)	-	201	-	-
Total research expenditure	**111,177**	**105,438**	**53,547**	**103,411**	**97,760**
Results from research activities	**2,785**	**(1,732)**	**1,924**	**(1,291)**	**(2,498)**
Other income					
Profit and loss on sale of long-term assets	8,671	9,512	2,170	5,324	21,600
Contribution income for recognition of land lease			-	-	-
Donations and bequests capitalised to Permanent Funds	5,162	719	137	1,581	219
Grants and donations for capital works	1,733	6,071	870	3,204	2,105
Total other income	**15,566**	**16,302**	**3,177**	**10,109**	**23,924**
Other expenses					
Loss on impairment write down of long-term investments	(709)	(4,808)	(391)	-	(263)
Depreciation and amortisation	(8,556)	(8,512)	(4,486)	(8,671)	(8,396)
Total other expenses	**(9,265)**	**(13,320)**	**(4,877)**	**(8,671)**	**(8,659)**
Net operating surplus	**9,086**	**1,250**	**224**	**147**	**12,767**
Capital funds					
Permanent invested capital funds	181,162	168,392	159,027	157,026	152,428
General funds	114,306	130,122	143,126	150,132	160,291
Royalty fund	34,981	26,169	24,387	19,994	17,551
Leadership fund	23,581	21,682	19,724	18,975	17,840
Discovery fund	2,682	2,362	2,109	2,030	-
Centenary fund	2,101	1,000	104	100	-
Investment revaluation reserve	34,393	35,305	47,755	46,763	31,165
Total funds	**393,206**	**385,032**	**396,232**	**395,020**	**379,275**
Capital expenditure					
Property, plant and equipment	**9,960**	**5,062**	**1,484**	**3,937**	**5,852**

Staff numbers: (equivalent full-time)	2016	2015	6 months to 31 December 2014	12 months to 30 June 2014	2013
Scientific research staff:					
– Senior faculty	78	79	77	78	76
– Postdoctoral scientists	188	176	190	197	186
– Visiting scientists	39	23	12	14	15
–Other laboratory research staff	252	238	269	265	268
Supporting staff:					
– Other support services	162	146	144	135	129
Total staff and visiting scientists	**719**	**662**	**692**	**689**	**674**
Students	**173**	**169**	**159**	**175**	**151**
Papers published	**429**	**410**	**167**	**381**	**298**

THE YEAR AT A GLANCE





The Year In Brief	2016	2015
Income for operations	**113,962**	**103,706**
Expenditure in operations	**111,177**	**105,438**
Net surplus (deficit) from operations	**2,785**	**(1,732)**
Number of staff and visiting scientists	**719**	**662**
Number of postgraduate students	**173**	**169**
Total staff and students (EFT)s	**892**	**831**

Walter+Eliza Hall
Institute of Medical Research

DISCOVERIES FOR HUMANITY

A beacon of hope

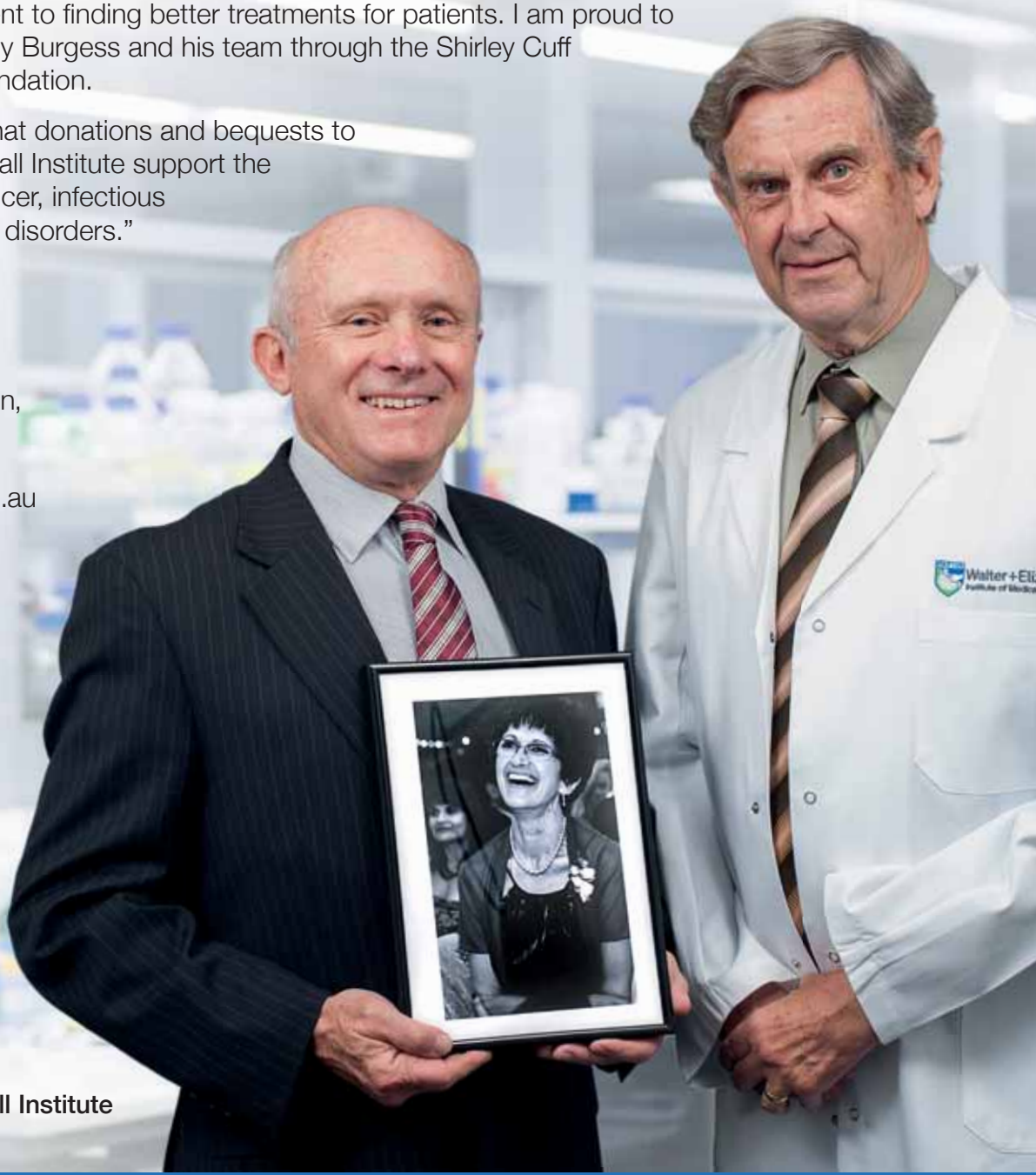
My involvement with the researchers at the Walter and Eliza Hall Institute of Medical Research has given me hope and purpose.

Thanks to the wonderful research underway at the Institute, I am confident that ultimately other families will not experience the devastating loss of a loved one to cancer.

When I met the scientists at the Walter and Eliza Hall Institute I was inspired by their passionate commitment to finding better treatments for patients. I am proud to support Professor Tony Burgess and his team through the Shirley Cuff Cancer Research Foundation.

You can be assured that donations and bequests to the Walter and Eliza Hall Institute support the best research into cancer, infectious diseases and immune disorders."

For more information please contact Ms Susanne Williamson, Head of Fundraising, on 03 9345 2962 or williamson.s@wehi.edu.au



Research advocate and donor Jeff Cuff, pictured with cancer researcher Professor Tony Burgess

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Walter and Eliza Hall Institute

CANCER | IMMUNE DISORDERS | INFECTIOUS DISEASE

EXTENDED ANNUAL REPORT

An extended version of the Walter and Eliza Hall Institute 2016 Annual Report is online at www.wehi.edu.au/annualreport-2016 and contains the full annual report as well as the following:

DOING GREAT SCIENCE

Scientific staff list

Attendance at major meetings

Full publications list

EXCEPTIONAL PEOPLE

List of PhD and Masters projects in progress

List of undergraduate trainees and visiting students

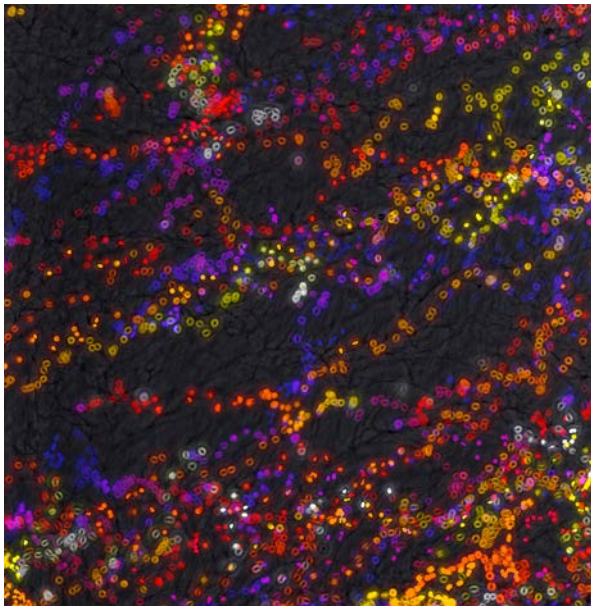
List of presentations that were given as part of our Institute Seminar program and Postgraduate Lecture Series

A SUSTAINABLE ORGANISATION

Full financial statements

Membership lists of Institute and board committees

Professional services staff list



Cover image

Art of Science finalist 2016

In search of influence
by Dr Joanna Groom
Molecular Immunology division

This mesmerising image has us searching for order as we try to trace the harlequin trails twisting and turning against the dark background.

The image is of immune cells – the tiny cells that defend our bodies from invading infection and disease. Immune cells are constantly moving around the body searching for signals that alert them to possible intruders, interacting with each other, ever ready to form a response. This experiment used time-lapse imaging to track the migration of immune cells for eight hours. Imaging software identified individual cell tracks and coloured the cells within these tracks. Such research helps scientists understand how cells use signals.