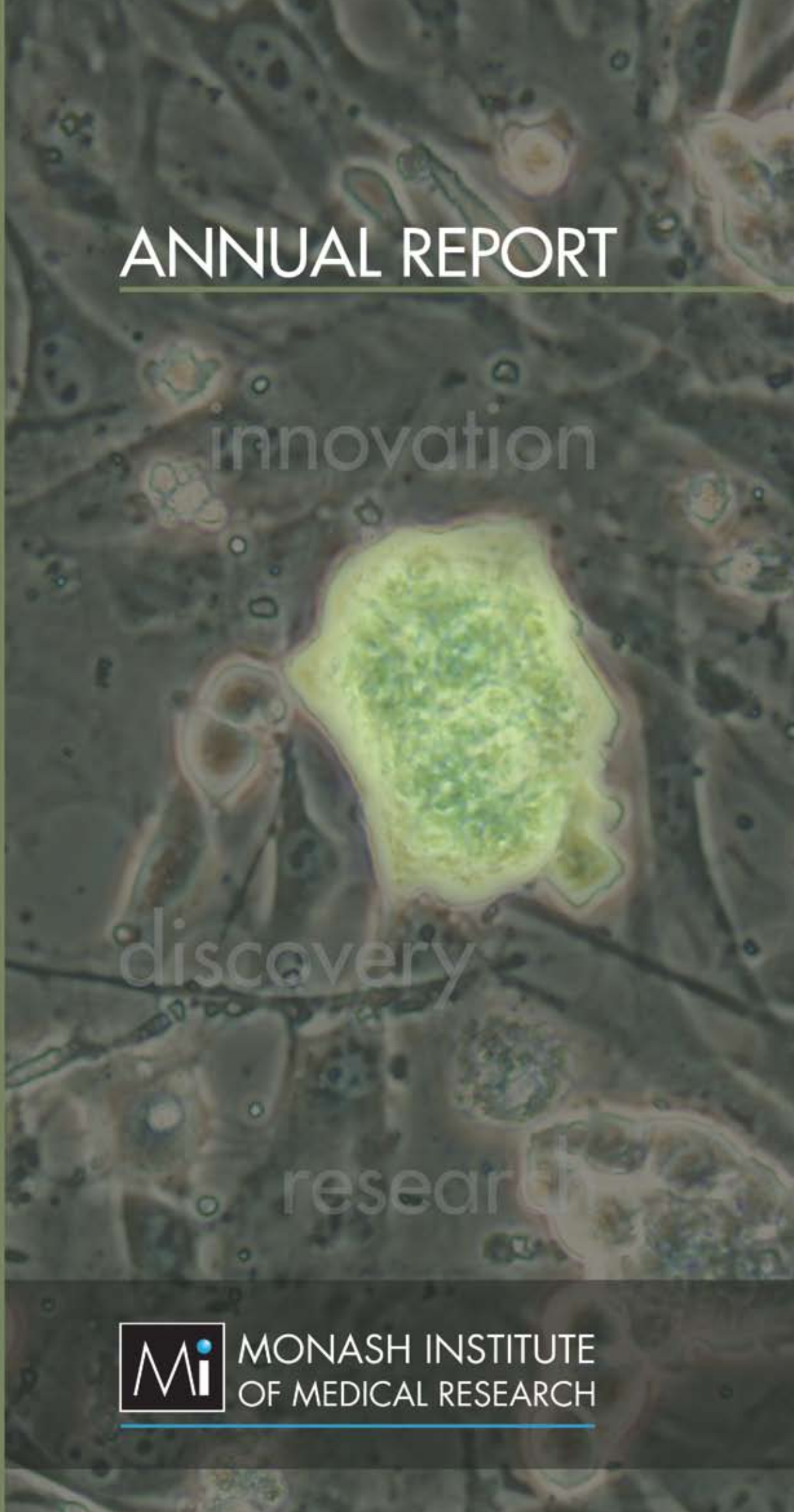
2007

ANNUAL REPORT



MONASH INSTITUTE
OF MEDICAL RESEARCH

As a major medical research institute,
MIMR will enhance human health and
the quality of life by major research,

innovation and discovery in biology,
medicine and biotechnology research.

CONTENTS

ABOUT MIMR

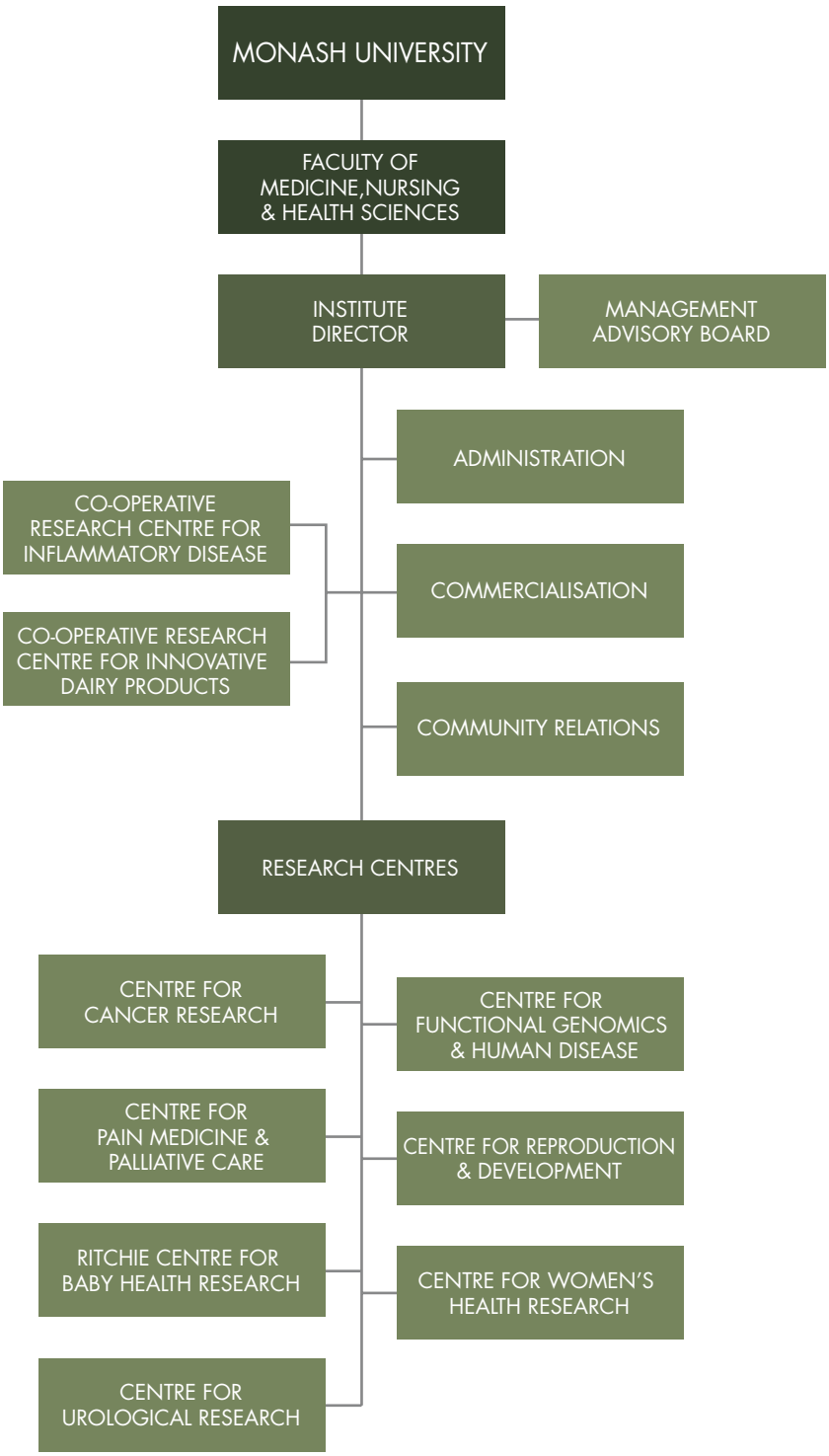
The Monash Institute of Medical Research was founded in 1991by Emeritus Professor David de Kretser AC. His passion for reproductive and developmental health was the driving force behind the formation of the then named Monash Institute for Reproduction and Development.

Throughout its short but dynamic history the Institute has evolved into an internationally recognised research institute, conducting world class research in seven research centres with a staff of 400 scientists and students.

While the original themes of fertility, preterm infant health and prostate cancer are still key research areas, the focus of MIMR has broadened to include research into cancer, inflammation and infectious diseases, women's health, stem cell biology, pain medicine and palliative care.

Professor de Kretser retired as Institute Director in 2005 to become the Governor of Victoria. In January 2006, Professor Bryan Williams, an internationally recognised cancer expert, commenced as Institute Director. Under Professor Williams' leadership, MIMR's reputation continues to grow as he oversees the next chapter of research, innovation and discovery.

ORGANISATIONAL STRUCTURE



DIRECTOR'S MESSAGE

This year has been one of expansion and growth at Monash Institute of Medical Research. We have taken major steps towards advancing our research. Each of the scientists, staff and members of the Management Advisory Board played an important role in fostering these developments.

The year began with the addition of our newest research centre, the Centre for Pain Medicine and Palliative Care led by Professor Colin Goodchild, Monash University's inaugural Professor of Anaesthesia. As the Australian population continues to age, the need for better understanding and treatment of chronic pain increases. The research conducted in this Centre has the potential to change the way we view and treat chronic pain in the community.

In April, we undertook a comprehensive scientific review of the Institute. Each Centre was reviewed on its research excellence, international competitiveness, opportunities for collaboration, uniqueness, vision and potential growth. The outcomes were insightful and encouraging and have provided some valuable strategic guidelines for planning for our future. I would like to thank our scientific reviewers who were so generous with their time to travel from interstate and overseas.

Throughout the year, our scientists made several discoveries that gained national and international exposure. This included our advances in stem cell biology, particularly in the area of women's health with the isolation of two types of stem cells in the endometrium. In addition, Prue Cowin, PhD student from the Centre for Urological Research, won the Bulletin Bayer Smart 100 Young Achiever of the Year award. Prue's talent and enthusiasm for her research is inspiring to all our scientists of the future.

We continued work on our commitment to expand international collaborations. A highlight of 2007 was a visit to Indonesia in May for the signing of a Memorandum of Agreement between MIMR, Monash University and Gadjah Mada University. This agreement paves the way for future joint research, staff development programs and student exchange.

In May, 40 members of the Thailand Medical School Executive visited MIMR to learn more about our medical education and research systems, as well as our administrative and quality processes.

We were visited by a delegation from India in July. The delegation included the Indian Minister for Health and Family Welfare and the Director-General of the Indian Council of Medical Research. India has a well established research program in adult stem cells and is looking to expand its endeavours into embryonic stem cell research and create links with MIMR to achieve this.

In August, the Canadian Minister for Health and his senior policy advisers visited MIMR, the Australian Stem Cell Centre and the Australian Synchrotron. His visit to Melbourne's south-east scientific hub was part of a nation-wide tour that also took in Sydney and the Cape York Peninsula, with the aim of creating more research collaborations and linkages between Canada and Australia.

Our fundraising efforts gained momentum. The Patrons Club continues to grow, as new alliances and networks are formed. In June, Patrons Club members were invited to a special evening which gave them the opportunity to participate in tours of our laboratories and to meet some of our scientists who were on hand to explain their latest research.

In November, we held our inaugural Ron Evans Golf Day, held in memory of an outstanding sportsman, family man, business man, philanthropist and Monash alumnus, who passed away on 9 March. More than 130 people gathered at the Royal Melbourne Golf Club to honour Ron and raise important funds for MIMR's cancer research. We are privileged that Ron's family chose to recognise his contribution to the community in this way.

The $125,000 raised on the day has been directed towards establishing the Ron Evans Cancer Research Fellowship. The Fellowship will be for an early-career scientist specialising in colon cancer research. Our heartfelt thanks and gratitude go to the Evans family, in particular Mrs Andrea Evans and her son David, for initiating this event and for their support of our research. Special thanks also go to the organising committee who worked tirelessly to make the day such a great success. The 2008 Golf Day has been booked and we hope it will be even better!

As the Institute expands, our need for increased infrastructure, equipment and funding to support new researchers also grows. Funding can be categorised into government funding, competitive research funding and philanthropic funding. We have attracted major competitive research funding which ranks us among the best in medical science across Australia. We have also been fortunate to gain funding through philanthropic organisations which has enabled the purchase of advanced technologies and the establishment of new research projects.

DIRECTOR'S MESSAGE

The importance of the support of the State Government cannot be over-emphasised. This support is critical to the survival of MIMR as it covers our day-to-day running costs. In addition, we continue to lobby both the State and Federal Governments for additional funding to develop our new building to house our ever-expanding research programs.

Professor Adrian Walker, founding member of the Institute and Director of the Ritchie Centre retired at the end of 2007. Adrian made an invaluable contribution as the Director of the Ritchie Centre, Executive Director of MIMR and Advisory Board member for many years. He was instrumental in fostering the careers of many young researchers, which was highlighted when he received the 2007 Supervisor of the Year Award from Monash University. We greatly value Adrian's contribution to MIMR and the work he did to improve the health of many babies born prematurely.

We welcomed the arrival of the new Dean of the Faculty of Medicine, Nursing and Health Sciences, Professor Steve Wesselingh. Formerly the Director of the Burnet Institute, Steve has a passion and vision for medical research that is shared by our Institute and we look forward to working with him.

I am continually impressed by the talents and calibre of the researchers at MIMR. Thank you to all scientists, staff and students who share the talent and passion that continues to drive MIMR to greater heights on an international scale.

Bryan Williams
Institute Director

CHAIRMAN'S MESSAGE

This year the Monash Institute of Medical Research (MIMR) has focussed on strengthening its reputation as a biomedical research centre of international stature. Increasingly, MIMR is engaged in translational research, whereby scientists' basic research is translated into improving patients' outcomes.

The Monash Health Research Precinct (MHRP) is a partnership between MIMR, Monash University, Southern Health and Prince Henry's Institute. The close relationship between Precinct partners is ideal for undertaking translational research. The exchange of ideas and knowledge between researchers and physicians encourages the development of improved treatments targeted to the clinical needs of patients.

By the beginning of 2007, the new MHRP building was fully occupied. However, further expansion is essential for the Precinct to continue to develop and extend its collaborative research activities. The current critical shortage of laboratory and clinical research facilities is constraining the innovative potential of the Precinct. Through its fundraising efforts, MIMR has generated vital seed funding for the next stage of the expansion project, but we need to continue to lobby both the State and Federal Governments for their support if we are to reinforce our links between laboratory and translational research and clinical trials.

MIMR also plays a vital role in the emerging Monash BioScience Cluster. This is a collection of institutes and organisations comprising medical and scientific institutes and schools within Monash University, the Australian Synchrotron, the Australian Stem Cell Centre, Prince Henry's Institute and the Alfred Medical

CHAIRMAN'S MESSAGE

Research Precinct. We have an invaluable opportunity to harness the wealth of talent, experience, resources and networks at our doorstep. By aligning MIMR with these key bioscience entities and promoting our collective scientific breakthroughs, we will raise our profile with the State and Federal Governments and with major philanthropic organisations.

The retirement of Professor Adrian Walker from the Institute's executive team and from his leadership role within the Ritchie Centre for Baby Health Research has marked the end of an era. I join with Bryan in congratulating Adrian on more than 35 years of dedicated research, leadership, teaching and student supervision. His impact on the lives of preterm babies and students will be a lasting one.

Professor Steve Wesselingh, the new Dean of the Faculty of Medicine, Nursing and Health Sciences, arrived late in the year, but has already made his presence felt. I know all at the Institute look forward to working with Steve.

2007 was another busy, rewarding year for MIMR Advisory Board Members, scientists, students and staff. I would like to congratulate Professor Bryan Williams on his exemplary leadership, and thank all involved for the scientific discoveries we continue to pioneer. It is an honour and a privilege to be part of MIMR.

George Pappas
Chair, Monash Medical Research Advisory Board

MANAGEMENT ADVISORY BOARD

Chair: Mr George Pappas

Senior Advisor, The Boston Consulting Group

Chair, Committee for Melbourne

Director, Western Bulldogs Football Club

Deputy Chair: Mr Rod Chadwick

Former Director, Managing Director and Chief Executive Officer, Pacific Dunlop Ltd

Advisory Board Member for Australia and New Zealand, Oracle Corporation

National Deputy President, Australian Industry Group

Ms Barbara Crook

Professor Nick Birrell

Professorial Fellow, Monash University Faculty of Medicine, Nursing and Health Sciences

Venture Executive, Innovation Capital

Founder and former Chief Executive, Credit Suisse Asset Management Australia

Professor Edward Byrne AO

Dean, Faculty of Medicine, Nursing and Health Sciences, Monash University

Non-Executive Board Member, Cochlear Pty Ltd

Board Member, Neurosciences Australia Pty Ltd

Deputy Chair, Neurosciences Victoria Pty Ltd

Governor, BHP Billiton Trustees

Sir Roderick Carnegie AC

Former Managing Director, Chief Executive and Chairman of CRA Limited (Rio Tinto)

Fellow of Trinity College, Melbourne

Patron, Australian Centre for Blood Diseases

Professor William Charman

Dean, Victorian College of Pharmacy

Chairman, Seeding Drug Discovery Funding Committee, Wellcome Trust

Professor Edwina Cornish

Deputy Vice Chancellor (Research), Monash University

Fellow, Australian Academy of Technology Sciences and Engineering

Director, Victorian Partnership for Advanced Computing

Former member, Prime Minister's Science and Research Council, ARC Board and CRC Committee

Mr Jerry Ellis

Chancellor, Monash University

Chairman, Landcare Australia Limited

Chairman, Future Directions International

Past Chairman, Broken Hill Proprietary Company Limited (BHP)

Board of Trustees Member, Eisenhower Exchange Fellowships

Professor Christina Mitchell

Head, School of Biomedical Sciences, Monash University

Member, Victorian State Government Science and Biotechnology Advisory Committee

GOVERNANCE

Dr Hugh Niall

Executive Director, Founding Director and past Chief Executive Officer, Australian Stem Cell Centre

Former Chief Executive Officer, Biota

Chairman of the Diabetes Vaccine Development Centre

Associate Professor, Medicine, Harvard University Department of Medicine, Massachusetts General Hospital, Boston, USA

Mr David Pitt

Vice President, Finance & Chief Financial Officer, Monash University

Fellow of the Australian Institute of Company Directors

Member, Association of Superannuation Funds of Australia

Former Director, Strategic Projects, Telstra

Ms Sue Renkin

Managing Director, Intuitively Focussed Pty Ltd

CEO, Open Family Australia Inc

Chair, Monash Centre for Synchrotron Advisory Board

Prime Minister's representative on Australian Bravery Council

Mr Robert Smorgon

Deputy Chair, Escor Pty Ltd

Director, Australian Council for Children & Youth Organisations Inc

Chair, MIMR Patrons' Club

Mr Robert Thomas

Senior Advisor, Citigroup Australia & New Zealand

Chairman, Heartware Limited

Chairman, Australian Wealth Management Ltd

Board Member, Virgin Blue Ltd

Chairman, Security and Derivatives Industry Association

Mr Colin Wise

Non-executive Chairman, St Barbara Ltd

Chairman, St Barbara Ltd Remuneration Committee

Non-executive Director, Southern Health

Chairman, Southern Health's Quality Committee

Fellow, Australian Institute of Company Directors

Fellow, Australasian Institute of Mining and Metallurgy

Professor Bryan Williams

Director, Monash Institute of Medical Research

Centre Director, Centre for Cancer Research

Member, Monash Health Research Precinct Management Committee

Member, Southern Health Research Advisory Council

Chair, Southern Melbourne Integrated Cancer Service Research Advisory Group

Member, Ministerial Taskforce on Cancer Research Working Party

Member, Victorian Cancer Agency Consultative Council

The Hon Michael Woolridge

Chair, Neurosciences Australia

Professor, Monash University Faculty of Medicine, Nursing and Health Sciences

Chairman, Ministerial Advisory Committee on AIDS, Sexual Health and Hepatitis

Former Commonwealth Minister for Health

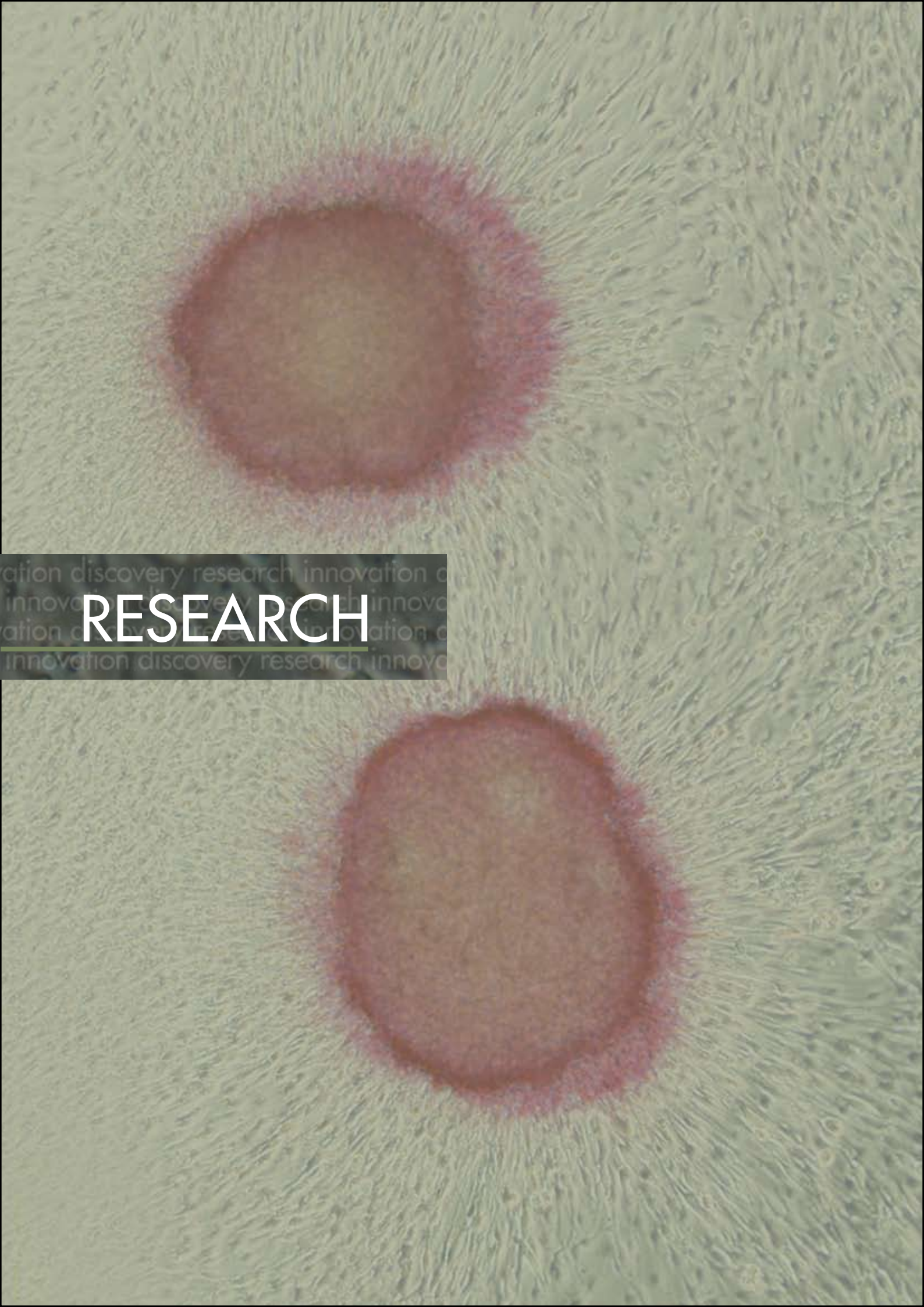
PATRONS

Sir Zelman Cowen AK, GCMG, GCOV

Governor General of Australia 1977 – 1982

Professor Richard Larkins AO

Vice Chancellor and President, Monash University


RESEARCH

CENTRE FOR CANCER RESEARCH

Institute Director and Centre Director: Professor Bryan Williams

Senior Scientist: Dr Elizabeth Williams

Scientists working in the Centre for Cancer Research are dedicated to studying basic aspects of cancer biology in an effort to learn more about the growth and development of different cancers and to translate their findings into new approaches to cancer prognosis and therapy. Scientists are particularly interested in the links between innate immunity, inflammatory processes and cancer and are developing a better understanding of cancer metastases and cancer-initiating stem cells.

There are close collaborations with scientists across MIMR and the Monash Health Research Precinct, on research into cancers of the breast, prostate, bladder, endometrium, ovary, stomach, head and neck, and kidney.

The Centre for Cancer Research team had great success in obtaining funding throughout 2007, with $2.7 million dollars received.

The Centre continued its rapid expansion in 2007, with the recruitment of three senior scientists: Professor Neil Watkins, from the Oncology Department at Johns Hopkins University, Baltimore, USA; Associate Professor Terry Johns, from the Ludwig Institute of Cancer Research; and Senior Research Fellow, Dr Greg Hannigan, from the Hospital for Sick Children, Toronto, Canada.

To accommodate the arrival of new staff members and their growing research teams, the Centre's research facilities are being expanded and improved. At the end of the year, the tissue culture room was demolished and a larger room built in its place. The new facility will be finished in April 2008, and will house nine class II biosafety cabinets and 16 incubators. Laboratories and offices are also being upgraded to ensure scientists have first-class facilities in which to undertake their research.

RESEARCH HIGHLIGHTS

Salicylates inhibit protein synthesis in a PERK-dependent manner

Salicylates, including aspirin, are used to treat a range of inflammatory conditions, and may be used to prevent diseases such as cancer. The effects of salicylates on the inhibition of protein synthesis, and the underlying molecular mechanisms involved were investigated. It was found that treatment of cells with salicylates induced phosphorylation of the eukaryotic translation initiation factor, eIF2α, and resulted in inhibition of the initiation of mRNA translation (and thus protein synthesis).

Under conditions of cellular stress, eIF2α is phosphorylated by stress-activated kinases such as protein kinase R-like endoplasmic reticulum kinase (*PERK*). It was found that salicylates caused an early increase in the phosphorylation of eIF2α in wild-type cells, but not in cells deficient in the perk gene. Salicylates were found to induce the activation of *PERK* in cells. Salicylates also inhibited protein synthesis in wild-type cells, but not significantly in cells deficient in the perk gene. Salicylates did not activate inositol-requiring enzyme 1. However, the expression of *CHOP(gadd153)* (a transcription factor produced in response to endoplasmic reticulum stress) increased in cells following treatment with salicylates. This up-regulation was partially *PERK* dependent.

Thus *PERK* plays an important role in salicylate-induced phosphorylation of eIF2α and the inhibition of protein synthesis. The research into the mechanisms involved in the action of salicylates may help in the design of drugs with more effective anti-proliferative activities.

Silva AM, Wang D, Komar AA, Castilho BA, Williams BRG (2007) Salicylates trigger protein synthesis inhibition in a protein kinase R-like endoplasmic reticulum kinase-dependent manner. *J Biol Chem* 282:10164-10171.

ATF3 negatively regulates TLR signalling pathways

Toll-like receptors (TLRs) recognise pathogen-associated molecular patterns, to activate the innate immune response. Activating transcription factor-3 (ATF3) is known to be induced by the activation of TLR4, and acts to negatively regulate TLR4 inflammatory responses in macrophages. In these experiments, it was shown that there was a much wider role for ATF3 in the innate immune response. Thus as well as being a negative regulator for the TLR4 inflammatory responses, ATF3 is a negative regulator for a number of other TLRs in mouse macrophages, and also regulates TLR responses in mouse and human dendritic cells.

Scientists found that levels of interleukin (IL)-12 and IL-6 stimulated by TLRs were increased in macrophages from mice deficient in the *atf3* gene compared to responses in wild-type macrophages. Thus ATF3 is a negative regulator of the expression of these interleukins. Also, the levels of IL-12 produced in response to TLR activation were increased in myeloid dendritic cells from mice deficient in the atf3 were challenged, compared to wild-type mice. Moreover, ATF3 antagonised the TLR-stimulated activation of the IL-12p40 promoter in a reporter assay. When mice deficient in the *atf3* gene with a TLR9 agonist, the production of cytokines in splenocytes increased. It was also found that the recovery in body weight following infection with influenza virus was delayed in mice deficient in the *atf3* gene compared to wild-type mice.

Thus ATF3 is a negative regulator of TLR signalling pathways, and deficiency in the atf3 gene affects immunological responses. This may have implications for diseases such as type I diabetes and cancer, as altered innate immunity may be involved in their pathogenesis.

Whitmore MM, Iparraguirre A, Kubelka L, Weninger W, Hai T, Williams BRG (2007) Negative regulation of TLR-signaling pathways by activating transcription factor-3. *J Immunol* 179(6):3622-3630.

 From left: Dr Elizabeth Williams, Prof Bryan Williams

COMMERCIALISATION

A USA Provisional Patent was granted in February 2007 to Dr Elizabeth Williams (co-inventor): *A method of treatment, prophylaxis and diagnosis and agents useful for same.*

GRANTS RECEIVED IN 2007

NHMRC Project Grants

BRG Williams
Functional analysis of relapse predictive genes in Wilms tumour (2008-2010)
$548,250

BRG Williams
Role of the IFN-induced helicase IFIH1 in type 1 diabetes (2008-2010)
$605,500

BRG Williams, M Wilce, J Wilce
Protein-RNA recognition in innate immunity (2008-2010)
$483,750

DL Russell, C Ricciardelli, ED Williams
Mechanism of breast cancer metastasis: tumour cell remodelling of the extracellular matrix (2008-2010)
$362,200

NHMRC Career Development Awards

ED Williams
How does cancer spread? (2008-2011)
$409,000

S Tong
The early origins of diseases in pregnancy; developing new predictive tests and biological insights (2008-2011)
$259,000

ARC Discovery Grant

MC Wilce, JA Wilce, M Gorospe, BRG Williams
Protein-mRNA interactions and their role in post-transcriptional gene regulation (2008-2010)
$719,500

ARC Linkage, Infrastructure, Equipment & Facilities Grant

P Hertzog, BRG Williams, J Rossjohn, B Adler, A Trounson, PM Sexton, MC Berndt
High content cell signaling discovery and screening facility (2008)
$350,000

Monash University Near-Miss Grant for NHMRC Project

ED Williams
Role of Pax6 and R-cadherin in bladder tumour metastasis (2008)
$20,000

RANZCOG Research Foundation, Arthur Wilson Memorial Fellowship

S Tong
Developing immunostimulatory RNA drugs that silence genes as treatment for cervical cancer and ectopic pregnancies (2008-2009)
$60,000

AWARDS RECEIVED IN 2007

Professor Bryan Williams
Bruce Cain Memorial Lecture for New Zealand Society Oncology Annual Meeting

Dr Michael Gantier
Travel Award, American Association for Cancer Research, AFLAC Incorporated

Dr Stephen Tong
NHMRC Achievement Award

Dr Elizabeth Williams
Travel Grant, Faculty of Medicine, Nursing and Health Sciences, Monash University

Dr Dakang Xu
Seymour and Vivian Milstein Travel Award, International Society for Interferon and Cytokine Research

CENTRE FOR FUNCTIONAL GENOMICS & HUMAN DISEASE

Centre Director: Professor Paul Hertzog

Senior Scientists: Dr Brendan Jenkins, Dr Ashley Mansell, Dr Bernadette Scott, Dr Trevor Wilson

Scientists working in the Centre for Functional Genomics & Human Disease investigate the molecular mechanisms of how the innate immune system is regulated to fight infectious diseases, inflammation, cancer and neurodegenerative diseases. The molecular pathways of particular interest involve interferons, toll-like receptors, the interleukin 6 cytokine family and their downstream effector proteins including STAT, NFκB and ETS transcription factors. By improving understanding of the molecular basis of disease and using cutting-edge technologies, scientists in the Centre hope to facilitate the development of new treatments and diagnostics for viral and bacterial infections, systemic infections and cancers of the stomach, mammary gland and mesothelium.

Throughout 2007, the Centre built on its role as a core member of the Cooperative Research Centre (CRC) for Chronic Inflammatory Diseases. Dr Trevor Wilson and Dr Bernadette Scott were promoted to project managers within the CRC. In partnership with AstraZeneca, CRC scientists continued to identify key targets for anti-inflammatory therapeutics. Partnership programs also included developing the validation of several new targets aimed at development of antibody-based therapeutics.

The Centre continued to lead several local and national initiatives. The Monash Infection and Immunity Network consolidated and raised the profile of Monash University's successful infection and immunity research. In addition, Dr Ashley Mansell, who created the TLROZ international network, convened the inaugural TLROZ conference.

RESEARCH HIGHLIGHTS

Pathological consequences of STAT3 hyper-activation by IL-6 and IL-11 during hematopoiesis and lymphopoiesis

Dr Jenkins and his team have previously shown in *gp130*$^{Y757F/Y757F}$ mice that a specific mutation in the gp130 receptor that is used by both interleukin (IL)-6 and IL-11 to generate intracellular signals leads to over-activation of the STAT3 latent transcription factor. These mice develop numerous haematological abnormalities, including elevated numbers of blood platelets (thrombocytosis) and neutrophils (neutrophilia), enlarged spleen (splenomegaly) and lymph nodes (lymphadenopathy). This study showed that genetic deletion of either IL-6 or IL-11 signalling in *gp130*$^{Y757F/Y757F}$ mice returned platelet and neutrophil numbers to normal, and this was associated with a normalised bone marrow compartment.

The elevated numbers of neutrophil precursor cells and megakaryocytes (platelet-producing cells) in bone marrow of *gp130*$^{Y757F/Y757F}$ mice was due to an increase in the STAT3-driven (by either IL-6 or IL-11) impairment of transforming growth factor (TGF) β signalling, which is a suppressor of these lineages. In contrast, the absence of only IL-6 prevented splenomegaly, lymphadenopathy and STAT3 hyper-activation in the spleen and lymph nodes of *gp130*$^{Y757F/Y757F}$ mice.

Furthermore, hyper-activation of STAT3 in these organs was associated with increased expression of the IL-6 binding receptor alpha subunit in a STAT3-dependent manner. Collectively, these data genetically define distinct roles of IL-6 and IL-11 in driving haematological disorders mediated by STAT3 hyper-activation.

Jenkins BJ, Roberts AW, Greenhill CJ, Najdovska M, Lundgren-May T, Robb L Grail D, Ernst M (2007) Pathological consequences of STAT3 hyper-activation by IL-6 and IL-11 during hematopoiesis and lymphopoiesis. *Blood* 109:2380-2388.

From left: Dr Trevor Wilson, Dr Ashley Mansell, Prof Paul Hertzog, Dr Bernadette Scott, Dr Brendan Jenkins

TGF-βRII rescues development of small intestinal epithelial cells in Elf3-deficient mice

Elf3, an *ets* transcription factor, regulates the activity of the transforming growth factor-β type II receptor (*Tgf-βRII*) gene. In a previous study the research team demonstrated that mice in which the *Elf3* gene had been ablated displayed a defect in the small intestine caused by a failure of small intestinal epithelial cells to differentiate. They also found that *Elf3* null mice expressed lower levels of *Tgf-βRII* protein, the *Tgf-βRII* gene product and potent inhibitor of cell proliferation and inducer of cell differentiation. This suggested that the defect observed in *Elf3* null mice resulted from the lack of *Elf3*-dependent activation of *Tgf-βRII* expression. To investigate this a genetic rescue was performed by restoring *Tgf-βRII* to *Elf3* null intestines.

The resultant *Elf3* null/*Tgf-βRII* transgenic mice displayed normal small intestinal morphology while the characteristic abnormality was retained in all *Elf3* $^{-/-}$ mice that did not express the *Tgf-βRII* transgene. This *in vivo* phenotypic rescue showed that a single gene, *Elf3*, is the critical upstream regulator of *Tgf-βRII* in mouse small intestinal epithelium. This has important implications for the understanding of tissue-specific gene regulation and further strengthens the potential clinical connection between *ELF3* and colorectal cancer involving TGF-β insensitivity.

Flentjar N, Chu P, Ng A Y-N, Johnstone CN, Heath JK, Ernst M, Hertzog PJ, Pritchard MA (2007) TGF-βRII rescues development of small intestinal epithelial cells in *Elf3*-deficient mice. *Gastroenterology* 132:1410-9

GRANTS RECEIVED IN 2007

NHMRC Project Grants

P Hertzog
New mechanisms of mediating interferon responses by trans-signalling (2008-2010)
$518,750

B Jenkins, P Bardin
Genetic approaches to understand how deregulated cytokine signalling drives the pathogenesis of emphysema (2008-2010)
$498,750

A Mansell
Suppression of immune toll-like receptor (TLR) signalling by hepatitis B e antigen (HBeAg) (2008-2010)
$520,500

ARC Linkage, Infrastructure, Equipment & Facilities Grant

P Hertzog, BRG Williams, J Rossjohn, B Adler, A Trounson, PM Sexton, MC Berndt
High content cell signaling discovery and screening facility (2008)
$350,000

Cancer Council Victoria

B Jenkins, A Mansell, R Ferrero
Cross-talk between cytokine and pathogen recognition receptor networks in the pathogenesis of gastric cancer (2008-2010)
$296,700

AWARDS RECEIVED IN 2007

Professor Paul Hertzog
Bursary, International Society for Interferon and Cytokine Research Conference

Dr Brendan Jenkins
Young Investigator Award, International Cytokine Society

Dr Ashley Mansell
Postdoctoral Travel Grant Award, CASS Foundation Ltd

Susie Noppert (PhD student)
Seymour and Vivian Milstein Travel Award

Dr Shamith Samarajiwa
Seymour and Vivian Milstein Travel Award
Scholarship to attend BioInfo Summer07, from the International Centre for Excellence for Education Mathematics

Connie Wong (PhD student)
Postgraduate Research Travel Grant and Study Away Award, Monash University International
Microcirulatory Society Zweifach Student Travel Award, 8th World Congress for Microcirculation

CENTRE FOR PAIN MEDICINE & PALLIATIVE CARE

Centre Director: Professor Colin Goodchild

The Centre for Pain Medicine & Palliative Care began in January 2007. The Centre's mission is to improve the quality of care provided to patients with pain and debilitating symptoms by promoting a multidisciplinary approach that advances research, education, clinical service and patient advocacy related to the medical specialities of pain medicine and palliative care. It is the Centre's ultimate aim to reduce the physical, psychological, social and economic burden produced by pain and distressing symptoms and related disorders.

Pain and other symptoms caused by acute and chronic illness should be managed by a system that receives input from multidisciplinary and multifunctional health professionals. The Centre for Pain Medicine & Palliative Care intends to develop positive patient outcomes by being the focus for integration of multidisciplinary Research and Education, and Clinical Service for Pain Medicine, Palliative Care and Anaesthesia.

Scientists in the Centre for Pain Medicine & Palliative Care have been conducting basic scientific research to develop new analgesic drugs for pain management. This laboratory research looks at drug combinations for pain syndromes, neuropathic pain, cancer pain and inflammatory pain. During 2007, the Centre has been involved in clinical trials for pain management in patients with cancer, HIV and diabetes. This research has been in close collaboration with CNSBio, a Monash University spin-out company. Several drugs are the subjects of research by this collaboration. These target a number of different elements involved with pain transmission and perception.

Of particular interest is the use of combinations of such drugs to maximise overall analgesic effect whilst at the same time minimising side effects. Several patents have been filed. The first patents from the collaboration have been published; those concerning flupirtine. This is a potassium channel opening drug that has been shown by the Centre to potentiate opioids in the management of neuropathic pain. The laboratory results have been translated into results in humans in a pilot clinical trial in patients suffering from neuropathic pain caused by advanced cancer. Further clinical trials are underway and more planned.

Prof Colin Goodchild

CENTRE FOR REPRODUCTION & DEVELOPMENT

Centre Director: Professor Michael Holland

Senior Scientists: Associate Professor Mark Hedger, Associate Professor Kate Loveland, Associate Professor Moira O'Bryan, Associate Professor David Phillips, Dr Paul Verma

The Centre for Reproduction & Development aims to apply knowledge derived from mammalian developmental and reproductive biology to practical problems in medicine and biotechnology. The Centre is focussed on the areas of assisted reproductive technology, male reproductive function, including endocrinology, infertility and contraceptive development, and animal biotechnology, including cloning and stem cell research.

2007 was an exciting year for stem cell research, following the Federal Government's decision in late 2006 to amend the stem cell laws. Dr Paul Verma was approached by the Indian Government to provide advice in the development of its stem cell research programs. India's large financial commitment to stem cell research will provide Dr Verma with the opportunity to undertake new projects and to access opportunities currently not possible in Australia. In July, India's Minister for Health and Family Welfare, the Honourable Dr A Ramadoss and the Director-General of the Indian Council of Medical Research, Dr NK Ganguly, visited the Centre with several other Indian Government officials to further discuss this partnership, which will soon be formalised in a Memorandum of Understanding.

Throughout 2007, scientists continued to strengthen their reputation for basic biotechnology research. This was highlighted with the Federal Government's announcement in March of a further $6.4 million in funding for a collaborative research project into male fertility, of which MIMR is a key partner. This allows MIMR and its project partners to continue this research until 2010.

Relationships with commercial partners, such as the CRC for Innovative Dairy Products, Genetics Australia and Schering, continued to flourish through increased emphasis on application as the outcome of basic research and a willingness to participate in the broad development of these applications.

From left: Assoc Prof Mark Hedger, Prof Michael Holland, Dr Paul Verma, Assoc Prof Moira O'Bryan, Assoc Prof David Phillips

RESEARCH HIGHLIGHTS

Cysteine-rich secretory protein 2 binds to mitogen-activated protein kinase kinase kinase 11 in mouse sperm

The cysteine-rich secretory proteins (CRISPs) are produced abundantly in the reproductive tract of all mammals. Due to this abundance, they are hypothesised to have an important role in the regulation of male fertility. However, data supporting this hypothesis remains limited. To investigate the biological function of the testis-enriched mouse CRISP2, yeast two-hybrid was used to screen a mouse testis expression library to identify binding proteins. These analyses identified mitogen-activated protein kinase kinase kinase 11 (MAP3K11) as a CRISP2 binding partner. The data indicated that CRISP2 present within the sperm acrosome, may be regulated by, or be involved in, the regulation of signalling cascades important for the activation of sperm required for fertilisation. Through generation of a series of CRISP2 deletion constructs, it was shown that this interaction was between the 60 carboxyl-terminal amino acids of CRISP2 and the 20 carboxyl-terminal amino acids of MAP3K11. This interaction was confirmed by pull down experiments using a recombinant CRISP2 C-terminal fragment. Furthermore, it was demonstrated that *MAP3K11* expression overlaps that of *CRISP2* within the testis, and that MAP3K11 protein undergoes N-terminal truncation within the testis, with the truncated form localised to the sperm acrosome. This overlapping localisation provides support for a relevant physiological interaction and supports the functional hypothesis.

Gibbs GM, Bianco DM, Jamsai D, Herlihy A, Ristevski S, Aitken RJ, de Kretser DM, O'Bryan MK (2007) Cysteine-rich secretory protein 2 binds to mitogen-activated protein kinase kinase kinase 11 in mouse sperm. *Biol Reprod* 77:108-114.

Activin A is a critical component of the inflammatory response, and its binding protein, follistatin, reduces mortality in endotoxemia

Activin is a protein found in many tissues that was originally described in the 1980s as a reproductive hormone. For around ten years scientists in the Centre have been working on a novel property of activin, notably that it is released into the bloodstream very rapidly following activation of the immune response in inflammatory syndromes such as septicemia. While it has been shown that this occurs in a sheep model of acute inflammation, and activin is elevated in a number of clinical inflammatory disorders, this paper showed a similar rapid release in mice, indicating that the activin response is highly conserved in evolution and part of the body's innate immunity.

Importantly, the effects of activin can be blocked by using a high-affinity binding protein, follistatin, which effectively neutralises the effect activin has on cells. By blocking the effect of activin using follistatin during acute inflammation, blood profiles of several key cytokines were modified. This showed that activin modifies the severity of the inflammatory response during these processes. Of major importance was the finding that using follistatin to block the activin effects during severe inflammation significantly reduced mortality. This indicated that follistatin could have therapeutic usefulness in clinical syndromes, such as septicemia, to aid in a patient's recovery from these devastating pathologies.

Jones KL, Mansell AS, Patella S, Scott BJ, Hedger MP, de Kretser DM, Phillips DJ (2007) Activin A is a critical component of the inflammatory response, and its binding protein, follistatin, reduces mortality in endotoxemia. *Proc Natl Acad Sci USA* 104 16239-16244.

Proteomic analysis of bovine conceptus fluids during early pregnancy

In cattle, early (day 45-90) loss of pregnancy is a common occurrence that leads to significant economic loss in both the dairy and beef industries. The ability to diagnose when pregnancies are at risk could lead to the development of intervention strategies to save the pregnancy or to terminate the pregnancy and allow the cow to conceive again. Unfortunately, there are no current data available on which this decision can be based. In light of this, a proteomic study was undertaken to map all proteins present at day 45 and day 90 in cows that were pregnant either by artificial insemination, IVF or via transfer of cloned embryos.

This was done using a combination of two dimensional electrophoresis and liquid chromatography/mass spectrometry. It was found that more than 200 proteins differed, 139 of which were identified. Scientists then sought to identify whether the presence or absence of specific proteins correlated with the pregnancy outcome. At day 45, significant differences in the protein profile of both amniotic and allantoic fluid were noted. No difference was seen at day 90. Further studies are now being conducted to see if the proteins are also detectable in serum, and if the physiological role(s) of the proteins can be identified.

Riding GA, Jones A, Holland MK, Hill JR, Lehnert SA (2008) Proteomic analysis of bovine conceptus fluids during early pregnancy. *Proteomics* 8:160-177.

COMMERCIALISATION

Provisional patent filed: *A method for producing stem cells or stem cell-like cells from mammalian embryos.* Co-inventor: Dr Paul Verma

The invention relates to methods and compositions for the production and derivation of pluripotent stem cells from embryos or embryo-derived cells and therapeutic uses. In particular, the invention relates to a method for producing functional stem cells or stem cell-like cells comprising the steps of culturing an embryo or embryo-derived cells in the presence of a demethylation agent and isolating functional pluripotent cells.

GRANTS RECEIVED IN 2007

NHMRC Project Grants

M O'Bryan
The identification of male meiosis genes using a new mouse line and human genome scans for gene copy number variations (2008-2010)
$580,500

M O'Bryan, K Jones
The function of gametogenin in male fertility and embryogenesis (2008-2010)
$516,000

ARC Discovery Grant

K Loveland, Y Miyamoto, N Hecht, Y Yoneda, M Handel
Novel roles for importin alpha proteins in the nucleus (2008-2012)
$885,000

NHMRC Training Postgraduate Fellowship

VJ Hall
Towards improving cell plasticity and developing autologous cell transplantation therapies (2008-2012)
$274,000

NHMRC Training Postgraduate Scholarship

C Heffernan
Deriving embryonic stem cell-like cells from manipulating normal adult cells (2008-2010)
$54,665

AWARDS RECEIVED IN 2007

Dr Gerard Gibbs
Junior Postdoctoral Travel Fellowship, Harold Mitchell Foundation

Dr Cathryn Hogarth
Travel Award, New Investigator Award, Society for Reproductive Biology

Dr Duangporn Jamsai
International Travel Award, American Society of Andrology
Travel Grant, Ian Potter Foundation

Mei Ling Lim (PhD student)
Society Poster Award, Asian Reproductive Biotechnology, Singapore

Dr Paul Verma
Visiting Professor, National Centre for BiologSciences (NCBS), Tata Institute of Fundamental Research (TIFR), Bangalore, India

Natasha Zamudio (PhD Student)
Lalor International Travel Award, American Society of Andrology

Promotions awarded in 2007

Professor Michael Holland
Appointed Deputy Director of the Monash Institute of Medical Research

Associate Professor Kate Loveland
Promotion to Associate Professor

Associate Professor Moira O'Bryan
Promotion to Associate Professor

RITCHIE CENTRE FOR BABY HEALTH RESEARCH

Centre Director: Professor Adrian Walker

Clinical Director: Professor Victor Yu AM

Scientific Director: Dr Philip Berger

Senior Scientist: Associate Professor Rosemary Horne

Scientists in the Ritchie Centre for Baby Health Research aim to prevent the death of babies and to improve their health through greater knowledge of the developmental physiology of the fetus and newborn.

Collaborative research based on partnerships between clinicians and scientists is the key strategy adopted by the Ritchie Centre to add to the body of knowledge relating to normal and abnormal growth and development of babies before and after birth, with a special focus on the key organs - the brain, heart and lungs.

The annual Kaarene Fitzgerald Lecture, jointly sponsored by SIDS and Kids, was held in October. One hundred and fifty members of the scientific community and the general public heard about the latest research in perinatal care, SIDS and children's sleep. This year's speakers were Professor Victor Yu, Ritchie Centre's Clinical Director and Professor Neonatology, Monash Newborn; Professor Adrian Walker, Director, Ritchie Centre, and Dr Gillian Nixon, Senior Research Fellow and Paediatric and Sleep Consultant at the Melbourne Children's Sleep Unit.

2007 marked the end of an era for the Ritchie Centre when founding Centre Director, Professor Adrian Walker, retired after 35 years devoted to studying the development of the fetus. To mark Professor Walker's significant contribution to medical research and MIMR, he was honoured with a Festschrift that brought together some of the world's most respected scientists and clinicians who reflected on the role he has played in shaping baby health research. Presentations by his students, past and present, testified to the broad scope of his contributions to perinatal research and medicine. As a fitting tribute to his dedication to fostering the talents of students, Professor Walker received the 2007 Supervisor of the Year award from Monash University.

From left: Dr Philip Berger, Assoc Prof Rosemary Horne

RESEARCH HIGHLIGHTS

How repeated exposure to hypercapnia affects arousal and cardiorespiratory responses during sleep

Arousal from sleep in response to potentially life-threatening dangers that prevent normal breathing is one of the most important protective mechanisms for the newborn infant. It is known that the arousal mechanism, and the cardio-respiratory responses it sets in train, rapidly become depressed in the active sleep state when episodes of hypoxia or asphyxia are repeated. Whether responses to repeated hypercapnia are similarly depressed has never been examined. In this study the arousal and cardio-respiratory responses were measured during repeated episodes of hypercapnia during sleep and the effect of repetitive stimulation was examined in both active sleep and quiet sleep to establish whether one of the sleep states is more vulnerable than the other. In eight newborn lambs studied over two successive 12 hour sleep recordings, spontaneous arousal probability was established before exposing the animal to a 60 second episode of normoxic hypercapnia (fractional inspired CO_2 = 0.08 and fractional inspired O_2 = 0.21 in N_2) during every quiet sleep and active sleep epoch. Lambs aroused far more often during the hypercapnic exposure than spontaneously during quiet sleep (58% versus 21%, Chi^2 = 54.0, $P < 0.001$) and active sleep (39% versus 20%, Chi^2 = 10.0, $P < 0.01$), though the response was less in active sleep. Exposure to hypercapnia also increased ventilation in quiet (150 ± 22%) and active sleep (97 ± 23%, $P < 0.05$), though the increase was smaller in active sleep ($P < 0.05$). Small (< 5%) blood pressure increases and heart rate decreases were evident during hypercapnia in quiet sleep, but not in active sleep. Repeated exposure to hypercapnia did not alter the arousal and cardio-respiratory responses. Unlike the loss of responsiveness that occurs with repeated exposure to hypoxia, the arousal mechanism and the cardio-respiratory responses that are elicited by hypercapnia, while less in active sleep than in quiet sleep, continue unabated with repeated exposure to hypercapnia.

Johnston RV, Grant DA, Wilkinson MH, Walker AM (2007) The effects of repeated exposure to hypercapnia on arousal and cardiorespiratory responses during sleep in lambs. *J Physiol (Lond)* 582:369-378.

Postnatal development of periodic breathing cycle duration in term and preterm infants

The duration of a cycle of periodic breathing, which consists of three to four breaths, alternating with a brief apnea, should increase with postnatal age or body size, according to theoretical models of respiratory control. Previous studies of periodic breathing cycle duration (PCD) with postnatal age in infants have yielded conflicting results. In term infants, PCD is reported to fall over the first six months postnatally, whereas in preterm infants it is reported either not to change or to fall. A large longitudinal study in 17 term and 22 preterm infants was performed. It was found that PCD decreased exponentially from birth in both groups, reaching a plateau between four and six months of age: PCD fell in preterm infants from 18.3 s to 9.8 s [95% confidence interval (CI) is ± 3.2 s], while in term infants, PCD fell from 15.4 s to 10.1 s (95% CI is ±3.1 s). It was interpreted that the higher PCD at birth in preterm infants, and the similar PCD value at 6 months in the two groups, is an indication of a more rapid maturation of PCD in preterm infants. This work provides strong support for earlier studies showing that PCD declines after birth. The disagreement between this data and theoretical predictions of PCD is evidence for there being important differences between the respiratory controller of the human infant and adult.

Wilkinson MH, Skuza EM, Rennie GC, Sands SA, Yiallourou SR, Horne RSC, Berger PJ (2007) Postnatal development of periodic breathing cycle duration in term and preterm infants. *Pediatr Res* 62:331-336.

COMMERCIALISATION

PulmoSonix

In partnership with Monash University, Premier Bionics Ltd (PBL) invested $2.5 million in 2002-4 to establish PulmoSonix Pty Ltd. The Ritchie Centre was awarded PulmoSonix research contracts for device development projects totalling $1.1 million in 2002-7.

Through its research contract with PulmoSonix, the Ritchie Centre has completed a large clinical study of a new medical device (AirwayClear) for diagnosis of obstructive sleep apnea in adults. A version of AirwayClear specifically designed for small infants is currently being tested in the Neonatal Intensive Care Unit of Monash Medical Centre.

A new device for early detection of emphysema is being tested clinically at the Alfred Hospital in a group of lung transplant patients with emphysema.

A further device to detect abnormal movement in the newborn infant, currently under trial in the Neonatal Intensive Care Unit of Monash Medical Centre, is being developed in association with the Howard Florey Institute and a commercial partner, Griffin Global.

GRANTS RECEIVED IN 2007

NHMRC Project Grant

RSC Horne, M Davey, G Nixon, J Trinder, S Hope, C Catroppa, D O'Driscoll
Impact of sleep disordered breathing on cardiovascular, behavioural and neurocognitive function in preschool children (2008- 2010)
$408,750

AWARDS RECEIVED IN 2007

Priscila Cassaglia (PhD student)
Travel Award, World Sleep Congress, World Federation of Sleep Research Societies

Bradley Edwards (PhD student)
Trainee Merit Award, World Sleep Congress, World Federation of Sleep Research Societies

Susan Feng (PhD student)
Trainee Merit Award, World Sleep Congress, World Federation of Sleep Research Societies

Simon Hew (BMedSci student)
Best Student Presentation, Healthy Start for a Healthy Life Conference, Melbourne

Heidi Richardson (PhD)
Senior PhD Student Travel Fellowship, Harold Mitchell Foundation
Travel Award, World Sleep Congress of the World Federation of Sleep Research Societies

Nicole Smith (PhD student)
Trainee Merit Award, World Sleep Congress, World Federation of Sleep Research Societies

Stephanie Yiallaourou (PhD student)
Travel Award, World Sleep Congress, World Federation of Sleep Research Societies

CENTRE FOR UROLOGICAL RESEARCH

Centre Director: Professor Gail Risbridger

Scientists working in the Centre for Urological Research (CURe) conduct basic and translational research that will provide better diagnosis, treatment and prevention of prostate diseases.

Prostate cancer is the most common cancer in Australia and is currently incurable if it spreads beyond the prostate gland. Scientists and clinicians working in CURe are developing a clear understanding of the features of prostate cancer biology, with the aim of discovering potential targets for clinical trials. While not life threatening, benign prostate hyperplasia (BPH) is an equally significant health problem. Ninety percent of all men aged over 80 have this condition that can have a dramatic effect on quality of life. Prostatitis, or inflammation of the prostate, is also non-life threatening, but causes debilitating pain.

During 2007, studies conducted at CURe in collaboration with toxicologists at the National Institute of Environmental Health Sciences in the USA showed that fungicides can cause prostatitis in young mammals. Prostatitis commonly occurs in younger men. The causes of prostatitis are not known in 95% of cases, so this is the first study to link prostatitis and exposure to environmental endocrine disrupting agents.

Studies were also undertaken to better understand hormone manipulation, which is the main treatment for prostate cancer and BPH. An ongoing challenge is to tailor therapies for BPH that would not exacerbate prostate cancer, and vice versa.

CURe scientists work closely with universities, hospitals and other research institutes in Australia and overseas to advance their research. The Centre is also affiliated with community education groups Andrology Australia and the Prostate Cancer Foundation of Australia. To complement their prostate cancer research, CURe has continued its role with the Australian Prostate Collaboration as the Victorian branch of BioResource, a national prostate tissue bank.

Prof Gail Risbridger

RESEARCH HIGHLIGHTS

Essential role for estrogen receptor ß in stromal-epithelial regulation of prostatic hyperplasia

In addition to the role of androgens, emerging evidence suggests that estrogens may also be important in the normal prostate as well as in the aetiology of prostate disease. Estrogens exert both direct and indirect effects on the prostate via the two estrogen receptors, ERα and ERβ, which are expressed locally within the tissue.

Previous studies have used animal models in an effort to dissect the role of ERβ, however they have been hindered by the centrally mediated response to estrogen administration (via ERα) that lowers androgen levels and ultimately masks any direct effects on the prostate mediated by ERβ. To overcome this inherent problem, the estrogen-deficient, aromatase knockout (ArKO) mouse was used in conjunction with tissue recombination. This work demonstrated that a deficiency in stromal aromatase – and thus local estrogen – led to the development of prostatic epithelial hyperplasia. Using an ERβ-specific agonist it was shown that ERβ is anti-proliferative and, once administered, that an ERβ-specific agonist did ablate this hyperplasia while an ERα specific agonist did not. Therefore, failed ERβ activation and increased androgen levels directly resulted in epithelial cell proliferation and ultimately prostatic hyperplasia. These data highlight the essential and beneficial effects of estrogens, necessary for normal growth of the prostate, as well as the potential of selective estrogen receptor modulators for the management of prostate growth and disease.

McPherson SJ, Ellem SJ, Simpson ER, Patchev V, Fritzemeier K-H, Risbridger GP (2007) Essential role for estrogen receptor β in stromal-epithelial regulation of prostatic hyperplasia. *Endocrinology*, 148:566-574.

Treating prostate cancer: a rationale for targeting local estrogens

Prostate cancer is the most commonly diagnosed cancer and the second most common cause of cancer-related deaths in men, while BPH is the most common benign condition known to occur in aging men. Androgen-deprivation therapy has been the mainstay therapy for prostate cancer, but is often insufficient due to relapse and progression of the disease to an androgen-independent state. Consequently, new options and targets for the treatment of these diseases are desperately needed.

Estrogens have been adversely implicated in the development and progression of prostate cancer, and offer a promising new avenue for the treatment of this disease. Despite this, the role of estrogens in the prostate is significantly complex, having both adverse and beneficial effects that are associated with the development of malignancy and prevention of hyperplasia, respectively. As both benign and malignant prostate diseases occur simultaneously in ageing men, the challenge is to block the adverse effects while promoting the beneficial effects. This article presents the basis of a targeted approach for the treatment of prostate disease through the use of selective estrogen receptor modulators in conjunction with contemporary androgen- deprivation therapy.

Ellem SJ, Risbridger GP (2007) Treating prostate cancer: a rationale for targeting local oestrogens. *Nat Rev Cancer*, 7:621-627.

GRANTS RECEIVED IN 2007

USA Army Medical Research & Material Command (DOD) Grants

Grant applications by CURe scientists to the US Army were ranked in the top eight percent of all grant applications in 2007.

G Risbridger
Endocrine disruption and human prostate cancer (2007-2008)
US $96,644

G Risbridger, R Taylor
Using human stem cells to study the role of the stroma in the initiation of prostate cancer (2008-2011)
US $464,646

S Ellem, G Risbridger
Linking estrogen, prostatitis and prostate cancer (2008-2009)
US $229,846

P Balanathan
New action of inhibin alpha subunit in advanced prostate cancer (2007-2008)
US $230,000

NHMRC Biomedical Fellowship

S Ellem
Linking estrogens, prostatitis and prostate cancer (2008-2011)
$209,250

Prostate Cancer Foundation and Cancer Australia
C Nelson, G Risbridger, J Clements, D Nicol, W Tilley
MicroRNAs in prostate cancer; novel biomarkers and potential therapeutic targets (2008-2011)
$648,000

Prostate Cancer Foundation Australia Young Investigator Grant

R Taylor
Molecular profiling and plasticity of prostate cancer stem cells with disease progression (2008-2011)
$300,000

Victorian Cancer Agency Early Career Seed Grant

R Taylor
Molecular profiling and plasticity of prostate cancer stem cells with disease progression (2008)
$50,000

GlaxoSmithKline Australia

P Balanathan
New action of inhibin alpha subunit in advanced prostate cancer (2008-2009)
$25,000

Faculty of Medicine, Nursing and Health Sciences, Monash University – Monash Strategic Grant

R Taylor
Manipulation of human embryonic stem cells to explore normal and malignant prostate differentiation (2008)
$35,000

AWARDS RECEIVED IN 2007

Dr Renea Taylor
Inaugural Monash University Distinguished Young Alumni Award
Finalist, Cure Cancer Foundation National Young Researcher of the Year

Prue Cowin (PhD student)
Bulletin Bayer Smart 100 Young Achiever of the Year
1st Prize, Third Year MIMR Postgraduate Student Symposium

CENTRE FOR WOMEN'S HEALTH RESEARCH

Centre Director: Professor Peter Rogers

Clinical Director: Professor Euan Wallace

Senior Scientist: Dr Caroline Gargett

Scientists and clinicians working in the Centre for Women's Health Research undertake clinical and fundamental research that will ultimately lead to better health outcomes for women. The Centre was created within Monash University's Department of Obstetrics and Gynaecology. Clinical and scientific staff share their knowledge, resources and findings, which helps drive a research focus on clinically relevant problems.

Research within the Centre can be divided into major themes or groups: endometrial biology (including stem cells, angiogenesis, endometriosis and breakthrough bleeding), maternal-fetal medicine (including placental function, amnion-drevived stem cells and predictors of adverse pregnancy outcome), infertility and IVF, and cancer biology (cancer of the endometrium, ovary and breast).

In 2007, scientists in the Centre for Women's Health Research generated $1.582 million in research income.

The inaugural Carl Wood Senior Lectureship in the Department of Obstetrics and Gynaecology was awarded in 2007. The Lectureship, supported by Monash University, commemorates Monash University's Foundation Professor in Obstetrics and Gynaecology. Professor Wood is Australia's best known specialist in infertility, IVF, fetal care and gynaecological endoscopy. The aim of the award is to nurture leaders in the demanding field of obstetrics and gynaecology.

There were two recipients in 2007; Dr Stephen Tong and Dr Gareth Weston. Dr Tong works in the Department of Obstetrics and Gynaecology and the Centre for Cancer Research. Dr Weston, an IVF specialist, is interested in female-specific reproductive ailments such as endometriosis and fibroids, which he believes are currently under-researched.

RESEARCH HIGHLIGHTS

Stem cells derived from human fetal membranes display multi-lineage differentiation potential

The amnion, the inner of two membranes surrounding the fetus, arises from pluripotent embryonic epiblast cells very early in gestation. As cells with stem cell-like properties may be retained even at the end of pregnancy, scientists investigated whether amnion membranes obtained after term delivery harboured cells with stem cell-like properties. Human amniotic epithelial cells (hAEC) isolated from term-delivered fetal membranes express mRNA and proteins present in human embryonic stem cells (hESC) including oct-4, sox-2, nanog, SSEA-4 and GCTM2. In keeping with possible stem cell-like activity, hAEC formed clonal colonies that could be expanded. The epithelial cells were also induced to differentiate into cell lineages derived from each of the three primary germ layers in vitro. The lineages derived included cardiomyocytes, myocytes, osteocytes, adipocytes (mesodermal), pancreatic and hepatic cells (endodermal), neurons and astrocytes (neuro-ectodermal).

The differentiated cells showed typical phenotypic characteristics, mRNA expression, immunocytochemical and/or ultrastructural features of these lineages. hAEC were also injected into testes of SCID mice. However, unlike hESC, hAEC did not form teratomas upon xeno-transplantation. Investigating their immune properties, it was found that only a very small proportion of hAEC contain human leukocyte antigens (HLA) Class IA and Class II antigens, implying a low risk of rejection following allogeneic transplantation. However, following differentiation into hepatic and pancreatic lineages, significant proportions of cells expressed HLA Class IA, but not Class II.

These findings suggest that the term amnion, a highly abundant and easily accessible tissue, may be a valuable source of multipotent stem cells that possess a degree of immune privilege and may be useful for stem cell-based therapies required for tissue regeneration and repair.

Ilancheran S, Michalska A, Peh G, Wallace EM, Pera M, Manuelpillai U (2007). Stem cells derived from human fetal membranes display multi-lineage differentiation potential. *Biol Reprod. 77*: 577-588.

Progesterone, but not estrogen, stimulates vessel maturation in the mouse endometrium

The endometrium (uterine lining) is one of the few adult tissues where significant blood vessel remodelling occurs on a routine, physiological basis. The blood vessels remodel during the menstrual cycle via the closely related processes of angiogenesis (new blood vessel growth) and vascular maturation (addition of support cells such as pericytes and/or vascular smooth muscle cells to the vessel wall). This study aimed to elucidate the effects of estrogen and progesterone on endometrial blood vessel maturation in mice. Endometrial tissues were collected from early pregnant mice (days 1-4) and ovariectomised mice treated with a single injection of 17β-estradiol (short-term estrogen regime) or daily injections of progesterone for three days (progesterone regime). In a further experiment, mice were treated concurrently with progesterone and either RU486 (progesterone receptor antagonist) or a vascular endothelial growth factor-A (VEGF-A) antiserum. Proliferation of vascular mural cells (PVMC) was observed on days 3-4 of pregnancy, when circulating progesterone begins to increase.

In the progesterone-treated mice, there was a significant increase in PVMC and α-smooth muscle actin (α-SMA, used to label mural cells) coverage of vessel profiles in comparison to controls. There were no significant changes in the mice treated with estrogen or the VEGF-A antiserum.

Unexpectedly, progesterone-induced increases in PVMC and mural cell coverage were not inhibited by RU486, although endothelial and epithelial cell proliferation was inhibited. These results show that progesterone stimulates vessel maturation in the mouse endometrium. These experiments demonstrate the importance of mechanistic studies using mouse models for understanding of endometrial vascular remodelling during the menstrual cycle.

Girling JE, Lederman FL, Walter LM and Rogers PAW (2007) Progesterone, but not estrogen, stimulates vessel maturation in the mouse endometrium. *Endocrinology* 148:5433- 5441.

From left: Dr Caroline Gargett, Prof Peter Rogers

GRANTS RECEIVED IN 2007

NHMRC Project Grants

E Wallace, U Manuelpillai, A Trounson, G Jenkin
Role of amnion derived stem cells in reducing lung fibrosis (2008-2010)
$335,500

H Parkington, E Wallace, G Jenkins, R Lang
Control of uterine contraction: role of interstitial cells (2008-2010)
$563,325

A Rumbold, J Boyle, S Kildea, E Wallace, R Thompson
Antenatal screening for fetal abnormalities in indigenous women: views of indigenous people and their health care providers (2008-2010)
$360,350

NHMRC Career Development Award

S Tong
The early origins of diseases in pregnancy; developing new predictive tests and biological insights (2008-2011)
$259,000

NHMRC Training Postgraduate Fellowship

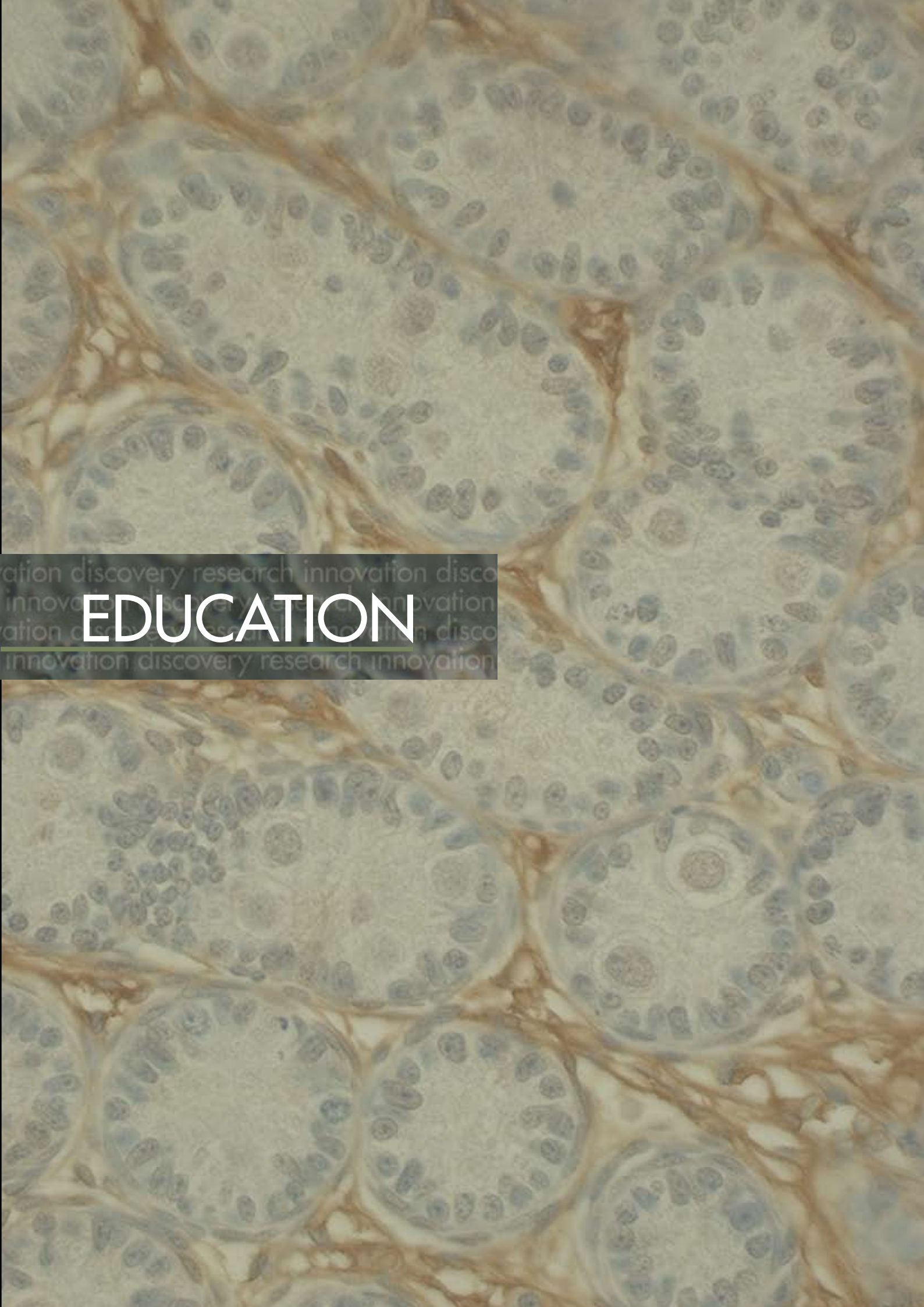
TJ Kaitu'U-Lino
The role of stem/progenitor cells in regeneration of mouse endometrium (2008-2010)
$274,000

NHMRC Training Postgraduate Scholarship

SR Hobson
Activin and endothelial dysfunction
(2008-2010)
$55,126

Cancer Council of Victoria

CE Gargett
Identifying markers of stem/progenitor cells in normal and malignant endometrium
(2008-2010)
$287,000


EDUCATION

EDUCATION

VISITING SPEAKERS

Dr Norman Hecht, University of Pennsylvania
William Shippen Jr. Professor of Human Reproduction, Department of Obstetrics and Gynaecology, USA

Post-transcriptional regulation by the DNA/RNA-binding protein MSY2 in mammalian germ cells (1/2/07)

Professor Christopher L Barratt
Institute of Biomedical Research, University of Birmingham, UK

The sperm cell - making the most of what you've got (22/2/07)

Dr Annemiek Nap
Department of Obstetrics and Gynaecology, Research Institute GROW, Maastricht University and University Hospital, Maastricht, The Netherlands

The pathogenesis of endometriosis; Sampson was right (27/2/07)

Professor Marco Cecchini
Department of Urology, University of Bern, Switzerland

Bone metastasis as an example of tumour-stroma interaction (8/3/07)

Professor Bryan Toole
College of Medicine, Medical University of South Carolina, USA

Targeting therapy-resistant cancer cells with hyaluronan-CD44 antagonists (15/3/07)

Dr Alejandro Tapia
Prince Henry's Institute

Leukaemia inhibitory factor: roles in placental development (27/3/07)

Professor Justin St John
The Medical School, University of Birmingham, UK

Mitochondrial DNA, why bother? (29/3/07)

Diana W Bianchi, MD
Vice Chair for Research, Floating Hospital for Children, Tufts University, Boston, USA

Pregnancy-associated progenitor cells: what stem cell researchers need to know (5/4/07)

Assistant Professor Neil Watkins
Johns Hopkins School of Medicine, Baltimore, USA

Hedgehog signalling in cancer (12/4/07)

Professor Ben Adler
ARC Centre of Excellence in Structural and Functional Microbial Genomics

Pasteurella multocida surface: structure, function and genetics (26/4/07)

Dr Ivan Bertoncello
Group Leader, Adult Lung Stem Cell Laboratory, Australian Stem Cell Centre

Isolation and characterization of candidate stem cells in the adult mouse lung (3/5/07)

Dr Louise Hull
Clinical Lecturer, Department of Obstetrics and Gynaecology, University of Adelaide

Tissue interactions during endometriotic lesion development (8/5/07)

Dr Helen Abud
Head, Epithelial Regeneration Laboratory, Department of Anatomy and Cell Biology, Monash University

The intestinal epithelium: approaches to studying conserved functions in a stem cell niche (15/5/07)

Regulation of stem cells in the mammalian gut (7/6/07)

Dr Helena Richardson
Group Leader, Cell Cycle & Development Laboratory, Peter MacCallum Cancer Centre

The neoplastic tumour suppressors, lethal-giant-larvae, discs-large and scribble in cell polarity, proliferation, apoptosis and tumourigenesis (17/5/07)

Professor Vicki Anderson
Theme Director, Critical Care & Neurosciences, Psychology Department, Royal Children's Hospital

The myth of early 'brain' plasticity? (24/5/07)

Dr John McKinlay
Senior Vice President and Chief Scientist, New England Research Institutes, USA

How much do we know about male reproductive health and how do we know it? Filling knowledge gaps with epidemiologic data (28/5/07)

Professor Sue Clark
Group Leader, Epigenetics Research Group, Cancer Research Program, Garvan Institute of Medical Research

Epigenetics and gene control: why is it important in cancer? (14/6/07)

Professor John Sedat
Group Leader, Nuclear Architecture and Chromosome Organization, University of California, San Francisco, USA

OMX, a new paradigm for wide-field optical microscopy (27/6/07)

Associate Professor Anita Corbett
Department of Biochemistry, Emory University School of Medicine, USA

Post-transcriptional regulation of gene expression (5/7/07)

Dr Bob Wong
Lecturer in Behavioural and Evolutionary Biology, School of Biological Sciences, Monash University

What females want (but don't always get): sexual selection in a freshwater fish (10/7/07)

Professor Judith Clements
Program Leader, Hormone Dependent Cancer, School of Life Sciences/IHBI, Queensland University of Technology

Kallikrein-related proteases in hormone dependent cancer (12/7/07)

Professor Rob Lewis
Director, Monash Centre for Synchrotron Studies, Monash University

The Australian Synchrotron in the imaging and diagnosis of cancer (2/8/07)

Associate Professor Robin Bell
Deputy Director Monash Medical School, Alfred Hospital Women's Health Program, Department of Medicine, Monash University

Ovarian health study (21/8/07)

Associate Professor Giovanna Zoccoli
Department of Human and General Physiology, Bologna University, Italy

Cardiovascular control during physiologic behaviour in hypertension (23/8/07)

Professor Phil Robinson
Head, Cell Signalling Unit, Children's Medical Research Institute

Dynamin's role in synaptic transmission: a target for new anti-epileptic drug discovery (30/8/07)

Dr Martin Matzuk
Stuart A. Wallace Chair, Department of Pathology, Department of Molecular and Cellular Biology, Department of Molecular and Human Genetics, Baylor College of Medicine, USA

Using genetic approaches to understand TGFbeta superfamily roles in reproduction (6/9/07)

Professor Terry Speed
Head of Division, Bioinformatics, WEHI and Department of Statistics, University of California, Berkeley, USA

Bioinformatics (13/9/07)

Professor Angel Lopez
Group Leader, Cytokine Receptor Laboratory, Hanson Centre for Medical Research, Adelaide

Cytokine receptor biology (20/9/07)

Professor Stephen Locarnini
Research and Molecular Development, Victorian Infectious Diseases Reference Laboratory

Pathogenesis of hepatitis B: new insights from studies of the innate immune response (11/10/07)

Professor Sandra Rees
Principal Investigator, Department of Anatomy and Cell Biology, University of Melbourne

Fetal and neonatal origins of altered brain development: implications for neurological disorders (23/10/07)

Dr Paul Hutchinson
Department of Immunology,
Monash Medical Centre

An introduction to flow cytometry at the Monash Institute of Medical Research (25/10/07)

EDUCATION

EDUCATION PROGRAM IN REPRODUCTION & DEVELOPMENT

Program Director: Associate Professor Peter Temple-Smith

The education program entered a new era in 2007 when the Faculty of Medicine, Nursing and Health Sciences approved a name change from the Education Program in Reproductive Biology to the Education Program in Reproduction & Development (EPRD). The new name reflects the broad research emphasis in MIMR on developmental biology and the changing content in EPRD postgraduate training programs.

In 2007, the strategic priorities for EPRD were to improve the program's course structures and administration and to design an off-campus version of the Master of Clinical Embryology (MCE) course for 2009.

It was a year of advancement and consolidation for EPRD, with increasing enrolments and continued high levels of teaching support from MIMR, Prince Henry's Institute, Monash Medical Centre and Faculty staff based on campus. Expanded and improved laboratory facilities and important upgrades in laboratory equipment continued to provide the programs with a strong competitive edge both nationally and internationally.

There was a robust teaching program in 2007. Seventeen students from 13 countries completed the MCE course. These students have gone on to work in IVF laboratories in Australia, New Zealand, Singapore, Thailand and the United Kingdom. One graduating student has been appointed to a lecturership in Nigeria, two are planning to pursue postgraduate research degrees and one has been accepted into a PhD program at the Monash Institute of Health Services Research.

Ten students completed the Graduate Diploma in Reproductive Sciences and nine students completed the Masters of Reproductive Sciences course in 2007.

International collaborations continued to strengthen. In January, Associate Professor Peter Temple-Smith, Dr Mulyoto Pangestu and Dr Sally Catt were invited to lecture at the Indonesian Endocrinology and Fertility Societies' Scientific Meetings in Yogyakarta, Indonesia.

In May, a high profile delegation from Indonesia's Diponegoro University's Faculty of Medicine visited EPRD to develop further collaborations in assisted reproductive technologies and infertility management training.

In August, four specialist trainees in obstetrics and gynaecology from Gadjah Mada University in Indonesia joined the MCE course for one month's training.

Through regular evaluation of course content, teaching and skills training, and through our workshops and collaborations, EPRD's international reputation will continue to grow in 2008 and beyond.

From left: Dr Mulyoto Pangestu, Dr Sally Catt, Assoc Prof Peter Temple-Smith, Dr Susan Cumming, Liz Doidge

LAUNCHING BIOTECHNOLOGY IN THE CLASSROOM

MIMR was proud to be associated with the production of a new biology resource for Year 12 students. Entitled *Biotechnology*, the textbook, published by Oxford University Press, brings real world, up-to-the-minute science directly into the classroom. MIMR Education Manager, Dr Susan Cumming, and Research Fellow, Dr Clare Borg, together with Dr Mary Vail, a Research Fellow from Monash University, co-authored the textbook.

The resource was launched in September by the Governor of Victoria, Emeritus Professor David de Kretser AC, who acknowledged the contributions of the authors and several recognised scientists from MIMR and other research institutes around Australia.

From left: Dr Mary Vail, Dr Susan Cumming, Emeritus Prof David de Kretser, Dr Clair Borg

PROFESSOR ADRIAN WALKER: SUPERVISOR OF THE YEAR

In his final year as part of the Monash community, it was appropriate that Professor Adrian Walker, retiring Director of the Ritchie Centre for Baby Health Research, was named the 2007 Monash Postgraduate Supervisor of the Year. Nominated by his own students, Professor Walker was selected from a large number of highly respected candidates from across all University faculties. He was committed to giving his students strong foundations for a successful career in medical research. It was fitting they were able to pay him this final tribute.

Prof Adrian Walker (centre), 2007 Monash University Postgraduate Supervisor of the Year

EDUCATION

STUDENT OPEN DAY

Recruiting enthusiastic, talented students to undertake postgraduate research at MIMR ensures the continued excellence in research at the Institute. To promote the diverse range of research opportunities, MIMR conducts an Open Day for potential students each year. Nearly 50 students attended the Open Day in August 2007, which was an increase in numbers from previous years. Final year PhD student, Heidi Richardson, gave a comprehensive overview of academic and social life at the Institute. Tours of each Centre were conducted and students had the opportunity to meet with some of the Institute's Senior Scientists.

Professor Michael Holland, Deputy Director, expressed his appreciation for Dr Ashley Mansell, Chair of the Student Open Day Committee, and all members of the Committee, who successfully managed this event for the Institute.

2007 STUDENT SYMPOSIUM

Invitrogen continued their generous sponsorship of this annual event, which provides PhD students with the opportunity to present their research to their peers and the Institute's Senior Scientists. The presentations were of an excellent standard and have set a high benchmark for students to achieve in the years to come.

The 2007 Student Symposium award winners were:

Team Player Awards:

1st Prize: Catherine Itman

2nd Prize: Rebecca Craythorn

3rd Prize: Badia Barakat

Third Year Presentation Awards:

1st Prize: Prue Cowin

2nd Prize: Vinali Dias

3rd Prize: Heidi Richardson

Fourth Year Presentation Awards:

1st Prize: Catherine Itman

2nd Prize: Camden Lo

3rd Prize: Sridurga Mithraprabhu

2007 GRADUATES

MIMR offers a range of Monash University Honours and postgraduate degrees.

The following students are to be congratulated for completing their studies in 2007:

PhD

Natalie Alexopoulos, Centre for Reproduction & Development: *Morphological assessment of pre-implantation bovine and ovine embryos post-transfer: implications for in vitro production and reproductive nuclear transfer*

David Aridi, Centre for Reproduction & Development: *Analysis of lymphocyte subsets in the rat and mouse testis and their immunoregulatory properties*

Megan Crane, Centre for Reproduction & Development: *Characterisation of immunosuppressive molecules of gonadal origin*

Cathryn Hogarth, Centre for Reproduction & Development: *Regulated importin expression throughout spermatogenesis*

Sivagami Ilancheran, Centre for Women's Health Research: *Stem cell properties of human amniotic epithelial cells*

Susie Noppert, Centre for Functional Genomics & Human Disease: *Role of type I interferon in LPS-mediated inflammation*

Gary Peh, Centre for Reproduction & Development: *Characterisation of neural progenitors from human embryonic stem cells*

George Riding, Centre for Reproduction & Development: *Proteomic studies of normal, IVF and cloned bovine pregnancies: differential analysis of the conceptus fluid proteome*

Kjiana Schwab, Centre for Women's Health Research: *Identification of markers for human endometrial stromal stem/progenitor cells*

Lisa Walter, Centre for Women's Health Research: *The molecular regulation of endometrial angiogenesis*

Marina Zaitseva, Centre for Women's Health Research: *Molecular investigation of factors that contribute to fibroid growth*

Master of Biomedical Science

Stephen Mandang, Centre for Women's Health Research: *Role of activin A in the pathogenesis of preeclampsia*

Bachelor of Biomedical Science (Honours)

Shirin Hussain, Centre for Urological Research: *Role of estrogens and estrogen receptor-β in the regulation of prostate growth*

Bachelor of Medical Science

Shavi Fernando, Centre for Women's Health Research: *Outcomes of assisted reproductive technology in women with endometriosis*

Master of Reproductive Sciences

Claire Walker, Centre for Women's Health Research: *Endogenous opioids at the maternal-placental interface during early pregnancy*

EDUCATION

Bachelor of Medical Science (Honours)

Sanja Coso, Centre for Cancer Research: *Vascular endothelial growth factor receptor-2 (VEGFR-2) signaling in prostate cancer - prostatic endothelial cell interaction*

Anthony Tachtsidis, Centre for Cancer Research: *Does R-cadherin play a role in tumour metastasis?*

Bachelor of Science (Honours)

Matthew Thompson, Centre for Cancer Research: *Characterizing the function of activating transcription factor 3 in Toll-like receptor signaling*

Lisa Xu, Centre for Cancer Research: *Functional characterization of the WT1 transcriptional target gene podocalyxin (PODXL)*

EDUCATION PROGRAM IN REPRODUCTION & DEVELOPMENT GRADUATES

Master of Clinical Embryology

Rubina Amin
Barbara Capstick
Asma Chhotani
Rabiu Inuwa
Itziar Rebollar Lazaro
Ismael Aguirre Maclennan
Fatima Momtaz
Dipali Patel
Sara Philip
Deepti Rampal
Padaphet Sayakhot
Pisit Tantiwattanakul
Naomi Maree Tappe
Sanyogita Tara
Meena Vahid
Xiaoqian Wang
Yee May Yap

Master of Reproductive Sciences

Farhat Bashir
Duyen Doan
Melanie Gibson
Kellie Hardy
Cameron Ingram
Michelle Ng
Deshira Saiti
Amanda Saltalamacchia
Jessica Thomas

Graduate Diploma in Reproductive Sciences

Mohd Banat
Lauren Bell
Natasha Dunn
Rebecca Epp
Jane Foley
Kai Lim
Krishna Mantravadi
Kheng Ling Ong
Ramya Sivanandam
Jaqueline Sudiman


COLLABORATIVE VENTURES

COLLABORATIVE VENTURES

CRC FOR CHRONIC INFLAMMATORY DISEASES

The Centre for Functional Genomics & Human Disease is one of four groups that form the CRC for Chronic Inflammatory Diseases, a national initiative comprising MIMR, the University of Melbourne, the University of Queensland and pharmaceutical company AstraZeneca (UK).

In May, Dr Ashley Mansell and Dr Trevor Wilson organised the first TLROZ conference at Bio21 in Melbourne. The meeting brought together Australian and international researchers to discuss the rapid progress in pathogen recognition; a review of the principal TLROZ findings was published in Nature Immunology and Cell Biology. The meeting was sponsored by the Australian Toll-like Receptor Network, MIMR and the CRC.

Two recent PhD graduates were offered prestigious international postdoctoral placements. Bioinformatician Dr Shamith Samarajiwa will take up a joint position at the Cancer Research Institute and the Department of Oncology, Cambridge University, UK. Dr Susie Noppert, supervised by Professor Paul Hertzog and Dr Ashley Mansell, completed her PhD thesis, *The role of interferon signalling in inflammatory responses*, and subsequently took up a postdoctoral fellowship in the Department of Nephrology, Medical University, Innsbruck, Austria.

The CRC has also continued to foster undergraduates through its Honours and Undergraduate Research Opportunities (UROP) Programs.

For postgraduates and early career researchers, career skills training (such as biostatistics, postdoctoral applications and grant writing) was undertaken at the annual retreat at North Stradbroke Island in March and at an intensive project management workshop in October.

The benchmark in the education program was the publication of *Biotechnology* (Mary Vail, Claire Borg and Susan Cumming, Oxford University Press, 2007), a supplemental textbook for Year 12 biology students and teachers. Dr Susan Cumming was awarded a contract from Biotechnology Australia for teacher professional development of *Biotechnology*; between September and December 2007, six workshops were held.

CRC FOR INNOVATIVE DAIRY PRODUCTS

The focus of the Education Program for the final year of the Dairy CRC was doctorate completions and postdoctoral placements, and ensuring a legacy to the Australian community from our school education biotechnology programs. A key form of support for postgraduate students completing their studies was the provision of research funding and the continuation of travel support to attend national and international conferences.

Three PhD theses were submitted. Dr Natalie Alexopoulos has taken up a Research Fellowship in the Department of Medicine (Neurosciences), Monash Medical Centre. Dr Ben Rollo is working in Professor Justin St John's Stem Cell Centre at the University of Warwick, United Kingdom. Dr George Riding, an external Monash PhD student who undertook his research in CSIRO Livestock Industries, is now using his skills in reproductive technologies on his own farm and remains working for CSIRO part time.

Ms Melissa Cooney, a CRC-funded PhD student, spent five months working in the University of Massachusetts' Amherst laboratory in the USA with Associate Professor Ralpael Fissore on activation of bovine and mouse oocytes by the bovine sperm protein PLC zeta. This work will contribute directly to her thesis.

Perhaps the most heartening evidence of the quality of postgraduates produced by the Dairy CRC Program is the winning of a Peter Doherty Fellowship by Dr Vanessa Hall, who did her doctoral work at MIMR and who is currently at the Department of Basic Animal and Veterinary Sciences, University of Copenhagen, Denmark. Dr Hall will return to MIMR in late 2008.

Our goal in the Schools Program was to 'contribute to a more informed and rational community debate about genetic technology issues, particularly in relation to the dairy industry'. This has been achieved by our two GenEd for Schools websites, and contributions to a textbook, *Biotechnology* (Oxford University Press, 2007). Through the Learning Federation, GenEd for primary (and lower secondary) schools will be accessed by all schools in Australia and New Zealand, thus ensuring a legacy to the community from Dairy CRC's Education Program.

COLLABORATIVE VENTURES

ANDROLOGY AUSTRALIA

Andrology Australia (the Australian Centre of Excellence in Male Health) is administered by MIMR and funded by the Australian Government Department of Health and Ageing. This national program continues to raise awareness of a range of men's health issues through community and professional education and support of research. In 2007, Andrology Australia experienced a period of review and recommendation, as well as forming important collaborations and completing a number of community and health professional education initiatives.

An independent panel of medical and health experts reviewed the achievements of Andrology Australia and noted the unique collaborative model of the program and the significant contribution being made to men's health in Australia. Also, an Advisory Forum highlighted the leadership position of Andrology Australia and outcomes from the meeting contributed to future strategy development.

Andrology Australia established collaborations with the Australian Prostate Cancer Collaboration (APCC) and Kinect Australia. Support of the APCC will contribute to improving prostate cancer research and education in Australia. Andrology Australia and Kinect Australia will work together to promote physical activity in men by raising awareness of reproductive health benefits.

A major achievement in community education was the development of the Men's Health Education Kit. The kit provides individuals and organisations with everything they need to hold a successful community seminar and raise awareness of men's health.

A series of GP summary guides, an online Active Learning Module on Younger Men's Health, and an Orchidometer (a set of sized models of testes, used for comparison of testicular development) were all produced in 2007 to further educate GPs in male reproductive health and assist them in the management of their male patients.


SUPPORTING OUR RESEARCH

SUPPORTING OUR RESEARCH

COMMERCIAL OFFICE

Following on the back of the strong research base underpinning the Institute, the Commercial Office played an important role in the transfer of technology and translational outcomes in 2007. Approximately $3.5 million in commercial revenues came into the Institute through various commercial activities including CRCs, contract research and licensing income. In terms of innovation, researchers at MIMR continue to add to future translational and commercial opportunities, with seven new invention disclosures and two new provisional patent applications being added to our existing patent portfolio.

MONASH HEALTH RESEARCH PRECINCT

The Monash Health Research Precinct (MHRP) brings together scientists from the Monash Institute of Medical Research, Monash University and Prince Henry's Institute with clinicians and patients from the Monash Medical Centre.

Close collaboration within the Precinct increases the impact of our research through translation of laboratory findings into improved clinical treatments. Precinct members share a number of resources and advanced facilities which further our research capacity.

Monash Gene Targeting Facility

The Monash Gene Targeting Facility was established in 2005 to provide MHRP researchers with gene targeting services in mice. The gene targeting facility provides a significant research tool in understanding gene function and studying human conditions. The Monash Gene Targeting Facility works by removing, altering or replacing a specific gene with a human equivalent, this state-of the art technology is furthering our research into respiratory diseases, embryo development, blood diseases, muscle development, the immune system and male infertility.

There are more than 20 concurrent projects ongoing for MIMR and other Monash University researchers. The Facility has expertise in molecular biology, embryonic stem cell growth and differentiation, micro-injection and animal husbandry.

Flow Cytometry Facility

The Flow Cytometry Facility provides diagnostic and research flow cytometry services for all scientists and staff at the Monash Health Research Precinct.

In 2007, a donation from the Pratt Foundation and the Jack and Robert Smorgon Family Foundation, enabled the purchase a flow Cytometer analyser (CyAn). The CyAn is a new generation, high-throughput, multi-channel unit that caters for sophisticated cell analysis and cell sorting requirements. It enables scientists to analyse the activation of cell signalling molecules at the single cell level.

Flow cytometry is a multifunctional tool that analyses complex cellular systems. It provides a highly sensitive method to identify, quantify and sort rare populations of cells/ This enables rare stem cells populations and minor immune cell populations, which have key roles in fundamental biological processes, to be studied.

The CyAn provides analysis of clinical samples which cannot be readily transported off-site and which often become available at unanticipated times. These include preparation of primary stem cells where delays of just minutes can affect their viability; and examination of early signalling events as soon as 10 minutes after stimulus.

From left: James Ngui, Lucas Law, Dale Carey, Dr Trevor Wilson, Dr Dirk Truman

SUPPORTING OUR RESEARCH

Gandel Charitable Trust Sequencing Centre

The Gandel Charitable Trust Sequencing Centre provides DNA sequencing services to MHRP researchers as well as external clients.

The Centre has the latest analytical technology and enables researchers to gain a greater understanding of gene structure and function. This information is integral to learning more about many human conditions, including cancer, Alzheimer's disease and infertility.

During 2007, the sequencing service experienced an increase in demand, with usage of the service by MHRP researchers and external organisations rising by 25 percent. In 2008, it is planned to further develop the services available with the extension of the real time PCR services.

Histology Laboratory

The Histology Laboratory caters to the immunohistochemical needs of scientists at MHRP and external clients on request. It offers a range of functions, including processing of electron microscopy and all aspects of paraffin, frozen and resin histology.

During 2007, the Histology Laboratory moved to an expanded location within the Monash Medical Centre, adjacent to the Ritchie Centre for Baby Health Research and the Centre for Women's Health Research. With the relocation of the service, a new tissue processor was purchased which has proved to be a valuable asset, allowing the laboratory to double its previous output.

Network Services, Monash Medical Centre

Network Services manage the information technology needs of all staff across the MHRP. The 2007 customer service report showed that the Network Services team continued to provide an efficient and effective service for all staff and students.

Animal Facilities, Monash Medical Centre

The Animal Facilities at Monash Medical Centre (MMCAF) provides vital support services to researchers across the Monash Health Research Precinct.

The facility breeds and cares for conventional mice, rats and sheep, as well as unique strains of specific pathogen-free (SPF) mice which require elaborate individually ventilated cages. Pigs and rabbits can also be accommodated within the complex.

During 2007, MMCAF was redeveloped and expanded to accommodate the growing needs of researchers across the Precinct.

ADMINISTRATION

Chief Operating Officer: Rod Wealands

In 2007, the Institute experienced a rapid expansion in research programs and staff. This growth impacted on the finance, human resources and logistics functions of the Institute.

The Administration team played a pivotal role in planning, designing and implementing the refurbishment of laboratories and office space to accommodate new staff and students.

The Human Resources department continued to conduct an orientation and induction program for all new staff and students.

As part of the Institute's commitment to staff wellbeing, the first Occupational Health and Safety (OH&S) Manager was appointed.

At the end of the year, the Administration team relocated to new office accommodation and the Logistics team moved into a purpose-built, centralised Store facility. In addition to providing much-needed space, the move also coincided with the implementation of an electronic archiving system and 'MOOS', an online ordering system. These new systems are part of the Institute's initiative to think 'green' and provide faster document retrieval and an improved ordering service for all scientists and staff.

Logistics Manager, Rod Gillett, was awarded the Dean's Award for Excellence for his outstanding service and leadership of the Logistics team.

SUPPORTING OUR RESEARCH

COMMUNITY RELATIONS & PHILANTHROPY

Manager, Marketing & Philanthropy: Sue James

Communications

MIMR's communications program publicises our scientists' work and aims to enhance the Institute's reputation for excellence in scientific research. Throughout 2007, the quarterly newsletter, MI News, highlighted key achievements and endeavours, and reported on the generous support provided by philanthropic organisations and individual donors.

In addition, local, national and international media reported on the groundbreaking work carried out in our laboratories, and journalists sought opinions and insight from our scientists and students.

From left: Julie Jacobs, Sue James, Susie Santilli, Andrea Carr

Community Support

Our scientists are highly successful in attracting major competitive research grants from organisations within Australia and overseas. However, the Institute depends on government infrastructure funds, philanthropic grants, donations and bequests to provide the equipment and research facilities that our scientists need for their work.

The Institute values the support it receives from Victorian State Government, through the Department of Innovation, Industry and Regional Development (DIIRD). As the Institute continues to expand, raising these funds is even more imperative.

The donations received from MIMR's appeals and the sale of Christmas cards to our supporters and through charity card shops throughout Victoria have contributed towards the purchase of vital equipment. We sincerely thank our donors for their ongoing support.

We continue to provide opportunities for Institute donors and support groups to tour the Institute to gain a greater understanding of our research programs and to meet our scientists. These 'Discovery Tours' provide supporters with a first-hand glimpse of scientific research and the opportunity to discuss this research with the scientists.

In October we were delighted to host the Rotary Club of Kew on Yarra for an evening tour, which culminated in a dinner at the Institute with Rotary members and their scientific hosts.

Institute scientists were regularly invited to present aspects of their research at speaking engagements to community groups and service organisations throughout the year.

Ron Evans Golf Day

In November the Institute conducted the inaugural Ron Evans Golf Day for Cancer Research at the Royal Melbourne Golf Club. The idea for the golf day was presented to the Institute by former Advisory Board Member Mr David Evans. We are most grateful to Mrs Andrea Evans and her family for choosing to honour Ron's contribution to the community through this golf day to raise funds for cancer research.

At the post-game dinner, Professor Bryan Williams, Institute Director, announced that the funds raised on the day would be directed towards the establishment of the Ron Evans Cancer Research Fellowship.

We acknowledge and thank the sponsors, the participating golfers and the organisations that generously assisted us to make this golf day a triumph. We look forward to conducting the second Ron Evans Golf Day for Cancer Research in November 2008.

Patrons Club

Members of the Patrons Club and WISE are an important part of the Institute's network. They act as advocates for the Institute in the wider community and their contribution and commitment is greatly valued.

The Patrons Club brings together people who are interested in supporting research conducted at the Institute and who enjoy the opportunity to develop a greater understanding of current research being carried out in their particular area of interest. WISE (Women In Scientific Excellence) brings together women who have a desire to assist early career female scientists reach their full potential in their research careers.

In June, Mr Robert Smorgon, Chair, Patrons Club, Professor Bryan Williams, Institute Director and Professor Richard Larkins, Vice Chancellor, President, Monash University and Patron of MIMR, hosted a 'scientific discovery' evening for members of the Patrons Club. Attendees had the opportunity to meet research groups in their laboratories, which was followed by refreshments and lively conversation with scientific staff.

SUPPORTING OUR RESEARCH

Patrons' Club & WISE Members 2007

Mr Ross Adler AC
Mr Ian Allen OAM
Ms Patricia Baitz
Mr John Baldwin
Mr Rex Beaconsfield
Mr Andrew Blode
Mr Mark Bryce
Mr Andrew Buxton
Ms Robin Campbell
Mr Colin Carter
Ms Mary Conigrave
Mr Frank Costa OAM
Mr Graham Crook
Mr Clyde Davenport
Emeritus Professor David de Kretser AC
Mr Ian Dicker
Mr Michael Drapac
Mr Les Erdi OAM
Mr David Evans
Mr Alan Finkel AM
Mr Barry Fradkin
Mr Peter Fraser
Dr Joel Freeman
Ms Vivienne Fried
Ms Alison Gargan
Ms Lauren Gargan
Mr Paul Gargett
Ms Ann Geddes
Ms Greta Grossberg
Ms Lanie Harris
Mr Dean Harris
Mr Anthony Heffernan
Ms Maureen Hindle
Ms Karen Joel
Ms Diana Jones AM, DSJ
Mr Craig Kimberley
Mr Ron Krongold
Mr Barry Landau
Mr Hylton Mackley
Mr Michael Naphtali
Mr Chris Pappas
Mr George Pappas
Mr Bruce Parncutt
Ms Marcia Pinskier
Professor Gail Risbridger
Mr Tony Rogers
Mr Steven Skala
Mr David J Smith
Mr David Smorgon OAM
Mr Jack Smorgon AO
Mr Michael Smorgon
Mr Norman Smorgon
Mr Robert Smorgon
Mr Stephen Smorgon
Mr Tony Smorgon
Mr Victor Smorgon AC
Mr Michael Sput
Mr Carl Strachan
Mr Rob Thomas

Ms Lisa Thurin

Professor Adrian Walker

Mr Peter White

Prof Bryan Williams

Mr Dennis Wilson

Mr Ross Wilson

Mr Graeme Wise

GE Healthcare

KI Scientific

Olympus Australia

Philanthropic Support

MIMR is sincerely grateful for the gifts received from individuals, trusts and foundations and organizations during the year. This valuable support assists the Institute to continue its important research.

The Institute acknowledges the following generous supporters.

Advanced Surgical Technologies

Allens Arthur Robinson

American Association for Cancer Research

American Medical Systems

ANZ Trustees Limited

Australian Anthill

Australian Football League

Australian Stem Cell Centre

B B Hutchings Bequest

Bayer Schering Pharma AG

Becco

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Bio-Rad Laboratories Pty Ltd

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Channel 9

Channel Seven Melbourne

Cricket Australia

Datasend Australia Pty Ltd

DOW Agrosciences Australia Ltd

Dubbo Prostate Cancer Support Group

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International Society for Interferon
Invitrogen Australia Pty Ltd
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L.E.W. Carty Charitable Fund
Linfox Airports
Massteknik Asia Pacific
Melbourne Aquarium
Millenium Science
Millipore Australia Pty Ltd
Minter Ellison
Mt Schanck Estate
Naphtali Family Foundation
National Australia Bank
Olympus Australia Pty Ltd
Ovarian Cancer Research Foundation
P & M Harbig (Holdings) Pty Ltd
Pacific Laboratory Products Pty Ltd
Plin Pty Ltd
RANZCOG Research Foundation
SIDS & Kids Victoria
Simon Beasley Racing & Sportsbet
SIRVA Insurance Centre
Spotless Group Limited
Ted's Camera Stores (Vic) Pty Ltd
The Apex Foundation Limited
The Cancer Council Victoria
The Cass Foundation Limited
The Endocrine Society of Australia
The Harry Secomb Foundation
The Ian Potter Foundation
The KDB Group of Companies
The Limb Family Foundation
The Marian & E H Flack Trust

The Michael & Andrew Buxton Foundation

The Parncutt Family Foundation

The Pratt Foundation

The Royal Melbourne Golf Club

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Anonymous

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Mr Ian Ball

Mr Anthony Barnes

Mr Clem Barrass

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Mrs Normie Bydder

Mr Douglas & Mrs Margaret Chandler

Emeritus Prof Arthur Clark AM

Mr Neville Clearson

Mr Arthur & Mrs Ethel Cocks

Mr David Cooke

Professor David Copolov

Ms Marion Coulson

Mr Graham Cowin

Mr John D'Arcy

Mr John Dixon

Mr Michael Drapac

Mr Ross Eddy

Mrs Andrea Evans

Mr David Evans

Ms Miriam Faine

Mr Peter Foster

Mr Ken & Mrs Shirley Fraser

Mr Graeme Fraser

Mrs Maya Friberg

Mrs Vivienne Fried

Mr Brian Gallery

Mr Paul Gargett

Mr PG Goldie

SUPPORTING OUR RESEARCH

Mr John Griffiths
Mr Kelvin Hack
Mrs Jean Hadges
Mrs A F Hamilton
Mr D Hammond
Mr Anthony & Mrs Lou Heffernan
Mr Rodney Hertzog
Mr Thomas Hogg
Mr Peter Hudson
Mr S.E.K. Hulme AM QC
Mr Georg Jaehrling
Mrs Sylvia Kemp
Mr Glen Kile
Mr Geoff Knorr
Mrs Leonie Koadlow
Mr Robert Liddle
Mr Otto Lobert
Associate Professor Kate Loveland
Mr Kevin Luscombe AM
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Mr Lance Matheson
Mr Ross & Mrs Margaret McCann
Mr Brian McCarthy
Hon. Allan W McDonald
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Mrs Jennifer Naughton
Mr Jim O'Connor
Ms Elizabeth O'Keefe
Dr Ruth Paluch
Mr George Pappas
Mr Ian A Parsons
Mrs Joanne Pearson
Mr Anthony H Pyman
Mr Alan J Reiter
Mr Ralph & Mrs Ruth Renard
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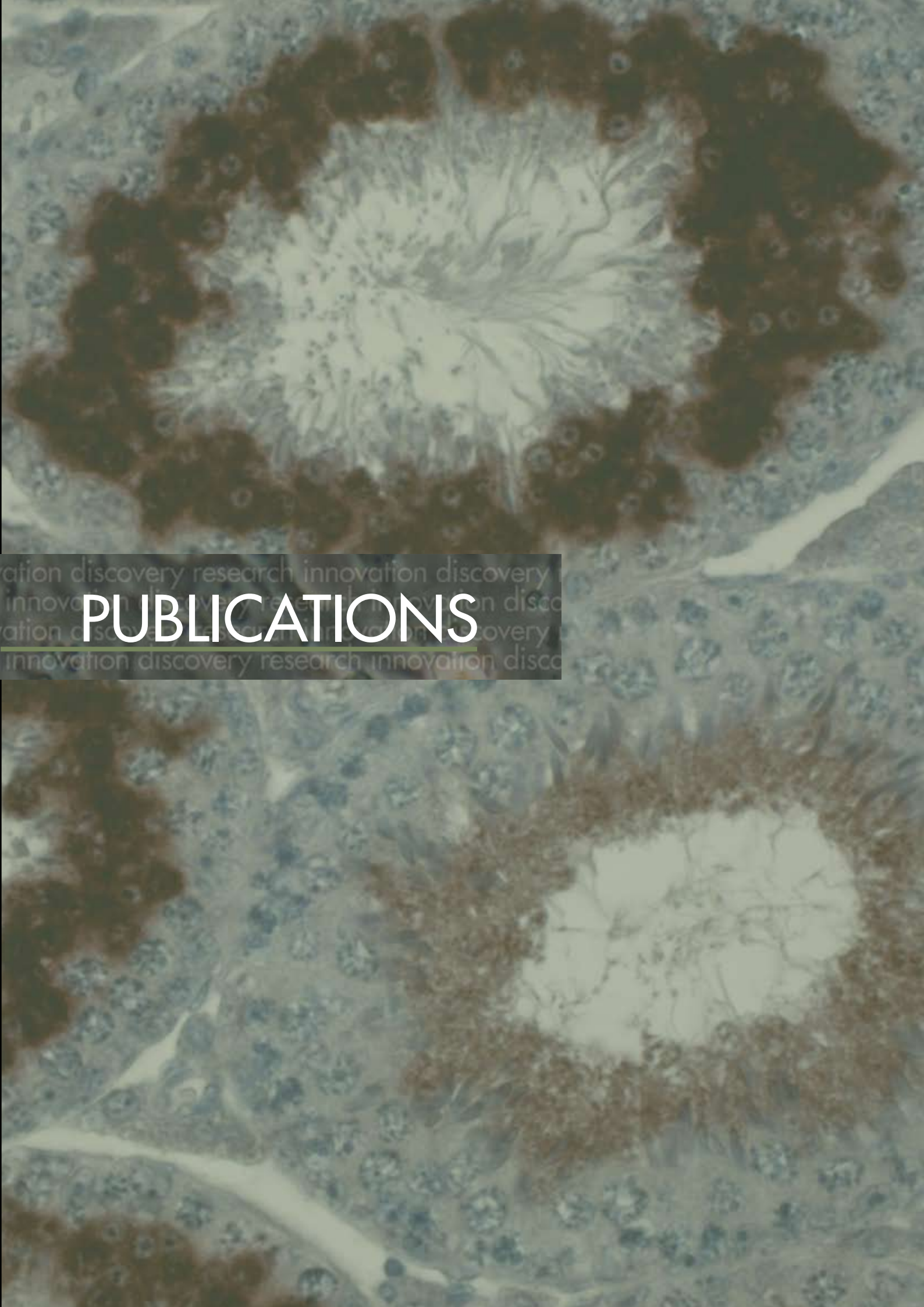
Mr Maxmilian Sachs
Mrs Barbara Schofield
Greg Shalit
Mr John Shalit
Mr Michael Slorach
Mr Keith Taylor
Mr Rob Thomas
Mrs Lisa Thurin
Mrs J R Tilley
Mr Don Upfill
Professor Adrian Walker
Mr Hugh Wallace
Mrs Baiba Warhaft
Mr George Wielgosz
Professor Bryan R G Williams
Mr John Williams
Dr Alex Wood
Ms Denise Young
Professor Victor Yu AM
Mr Laurence & Mrs Frances Zarth

Memorial Gifts

M Lee Cheong Yuen


PUBLICATIONS

PUBLICATIONS

CENTRE FOR CANCER RESEARCH

Journal Articles

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RITCHIE CENTRE FOR BABY HEALTH RESEARCH

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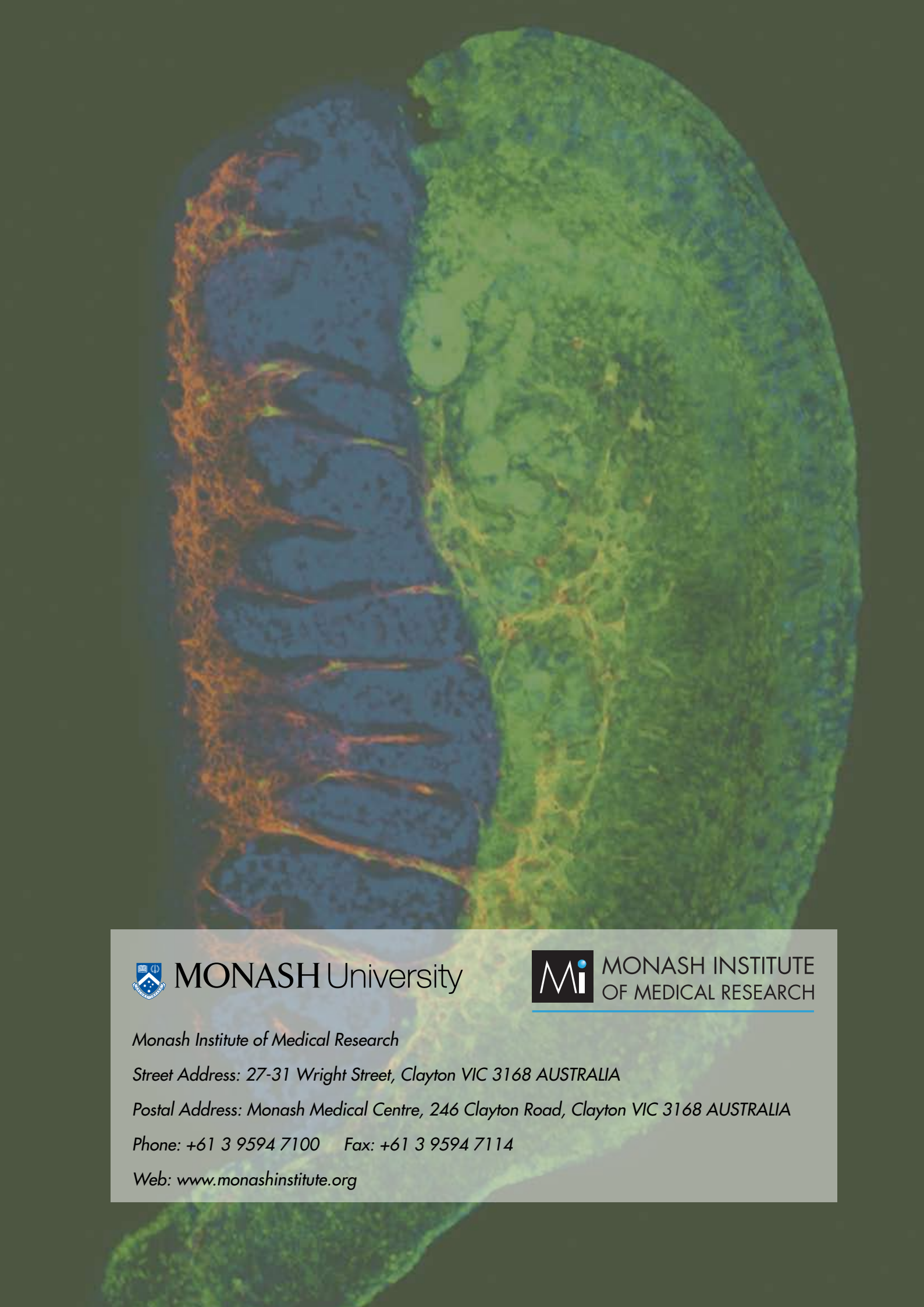
CASH FLOW STATEMENT

CASH FLOW STATEMENT

MONASH INSTITUTE OF MEDICAL RESEARCH

Cash Flow Statement Year to Date 31 December 2007

	2007
Previous Years Funds	
Previous Years Balance	1,126,366
Income	
General Revenue	5,292,190
Other Income	981,801
Commercial Services Income	239,221
Other Fees	
Student Course Fees	37,000
Investment Income	105,957
Non Research Funding	1,341,526
Scholarships & Prizes	6,298
Research Income	11,638,024
	19,642,017
Salaries Expenditure	
All Salary Expenses	11,962,443
	11,962,443
Non Salary Expenses	
Other Expenses	1,010,051
Financial & Admin Services	285,430
Travel & Related	729,611
Book & Library	71,817
Print & Stationery	422,630
Computer Related	322,210
Communications	222,998
Equipment Related	135,336
Lab & Operating	2,650,516
Student Related	437,624
Staff Related	9,146
Motor Vehicle	38,056
Building & Property	141,057
	6,476,482
Capital Expenditure	
Capital Expenditure	1,063,463
Year End Position	1,265,995



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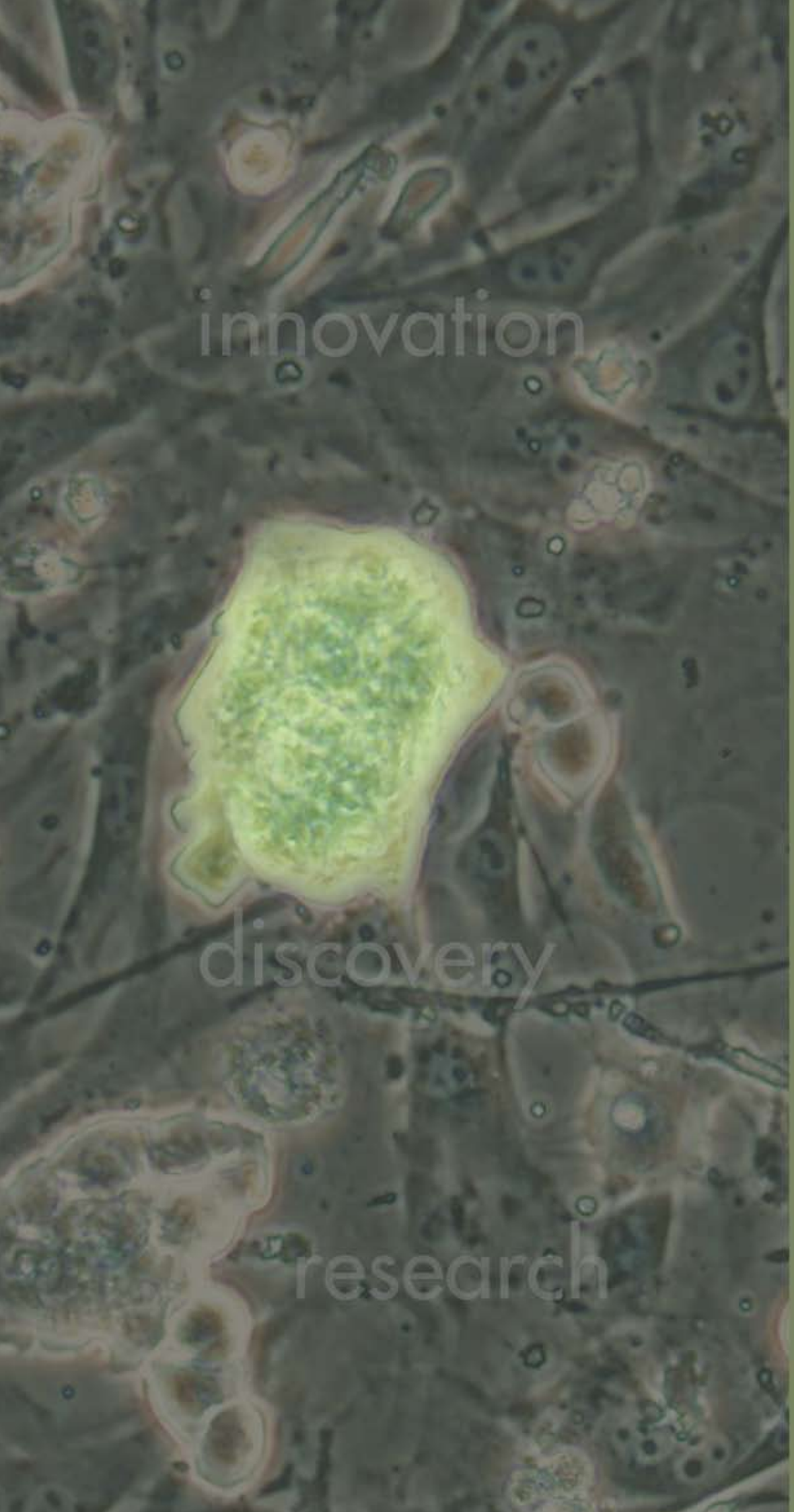
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