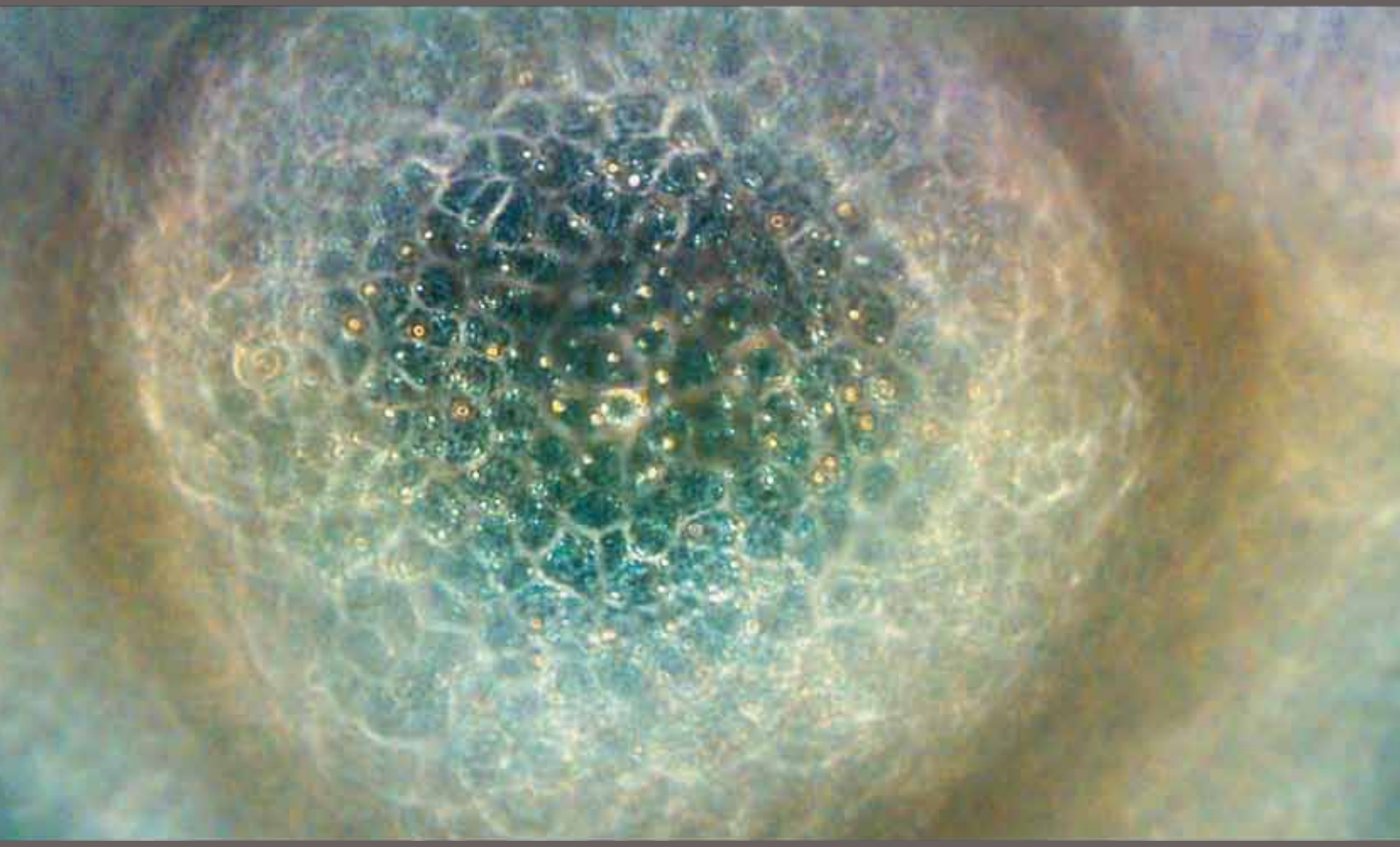
Annual Report



2008

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.

Vision

Cover image: Ectodermal cell outgrowths from a bovine (cow) embryo. Image taken by Dr Nadine Richings, Centre for Reproduction & Development

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About MIMR

Professor David de Kretser established the Monash Institute of Reproduction and Development (as it was originally known) in 1991. This Institute brought together scientists and clinicians undertaking research into conception, birth and development at the Centre for Early Human Development, Monash Medical Centre, with scientists working in the field of male reproductive health at Monash University's Department of Anatomy.

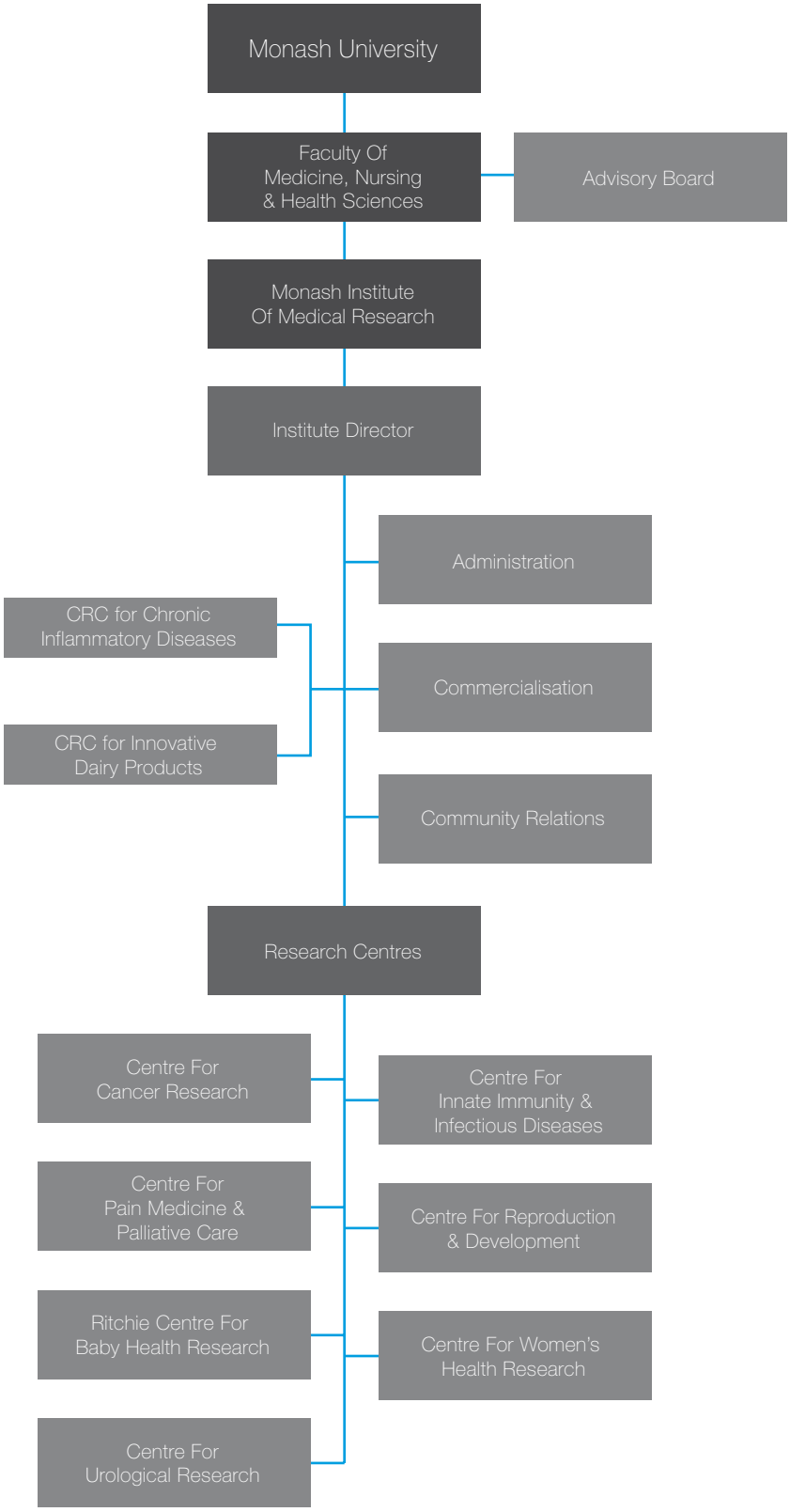
Over the years, the research conducted at the Monash Institute of Reproduction and Development (MIRD) benefitted many Australians, including infertile young people, parents of premature babies, and men with prostate cancer.

Recognising that its research had evolved beyond reproduction and development, MIRD became the Monash Institute of Medical Research (MIMR) in 2005. Today, MIMR is an internationally recognised research institute, conducting world class research in seven research centres with a staff of over 400 scientists and students.

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

Following Professor de Kretser's retirement in 2005, 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

'From bench to bedside' is a common phrase used to describe translational research, but it does not describe the full extent of the research life cycle. Translational research is more a two-way street. Successful translational research involves ongoing collaboration between scientists and clinicians. In addition to basic research, the bench to bedside journey also includes a complex maze of policies, disease modelling, and therapeutic and clinical trials. It is this two-way street that MIMR has continued to map and navigate throughout 2008.

Our collaborations opened up new avenues with an international agreement signed between MIMR and the University of Manitoba, Canada. Together, we have established world-first gene-targeted mouse models to determine links between inflammation and cancer. We are aiming to identify genes involved in the progression of cancer and develop diagnostics and early intervention therapeutics to stop cancer growth. We are looking forward to this partnership developing and seeing our research come to fruition.

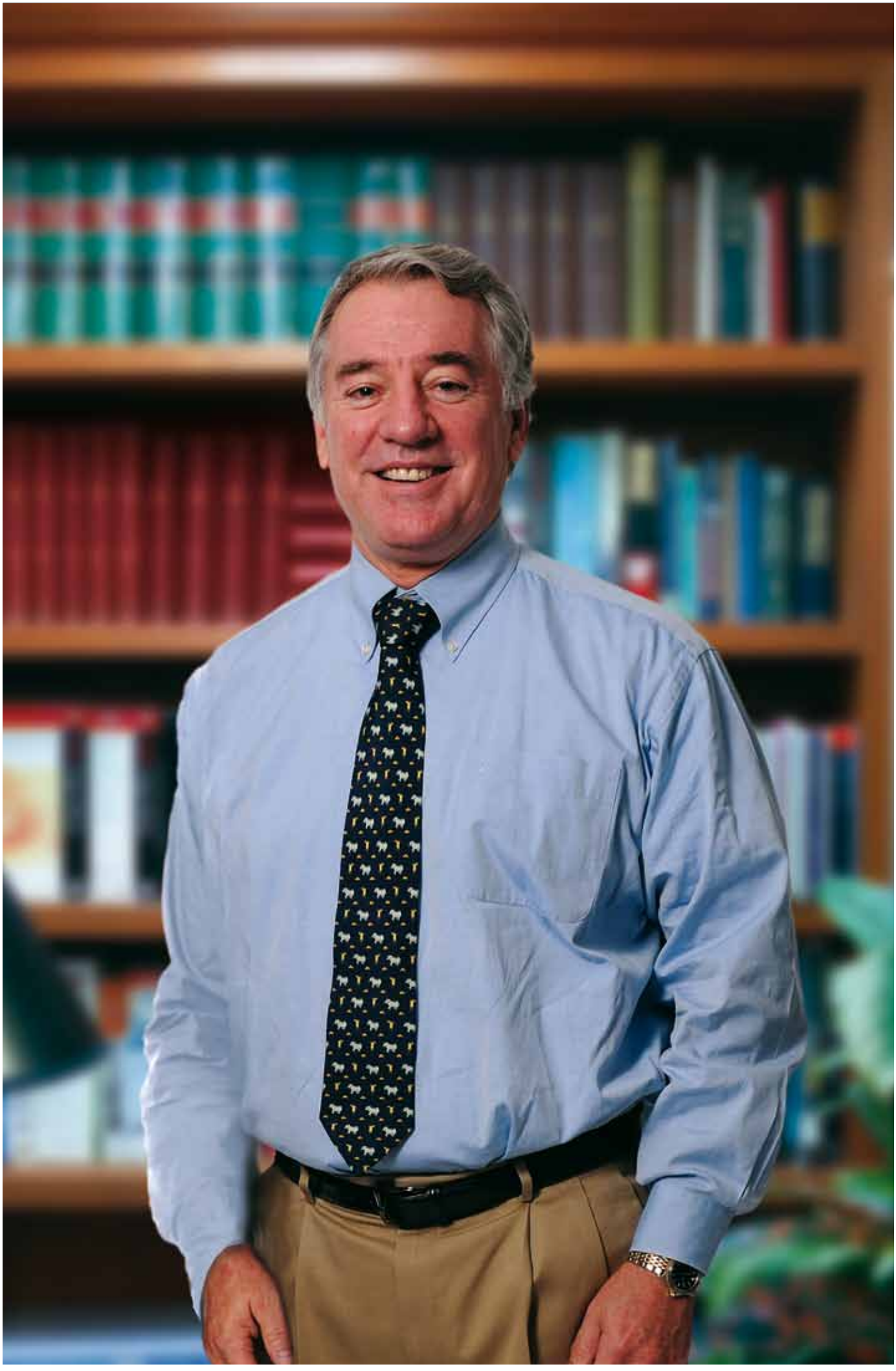
We could not operate as an Institute without the Victorian State Government's ongoing commitment to biomedical research through the Department of Innovation, Infrastructure and Regional Development (DIIRD). We were fortunate to receive an increase in funding this year, which was a reflection of our increased research output. DIIRD also funded a project in collaboration with the NSW State Government. Led by Dr Paul Verma, the project is aiming to create stem cells that may provide an alternative to embryonic stem cells. Although in its early stages, Paul has successfully created the first induced pluripotent stem (iPS) cell line in Australia using human adult skin cells.

We are also strengthening collaborative ties within the Institute. To encourage this, I was pleased to launch the MIMR Flagship Program; an internal initiative that encouraged our scientists to identify a project of high scientific and medical significance that will result in significant positive outcomes for patients. Scientists had to demonstrate a collaborative partnership with colleagues across different research areas. Inaugural recipients, Dr Elizabeth Williams, from the Centre for Cancer Research, and Dr Renea Taylor, from the Centre for Urological Research, will investigate genes involved in the suppression of an advanced type of prostate cancer. This will not only teach us more about the disease, but may also have implications for other cancers. My thanks go to Dr Philip Berger, who chaired the Project Committee, Emeritus Professor David de Kretser, who chaired the selection panel, and to our panel members.

Our researchers continued to shine on the national and international stage. Dr Stephen Tong was one of only 16 young Australians to receive a National Health and Medical Research Council (NHMRC) Achievement Award for Career Development; Associate Professor Moira O'Bryan was named Young Andrologist of the Year; Dr Nancy D'Cruz's research into the effects of cryopreservation on dairy cattle embryos was recognised with an Australian Agricultural Industries Young Innovator and Scientist Award; and Professor Gail Risbridger was awarded Honorary Life Membership of the Endocrine Society of Australia. In addition, Associate Professor Mark Hedger and Dr Caroline Gargett were two of only ten Australians to be recognised in the NHMRC's '10 of the Best', which highlighted the top ten medical research projects in Australia funded by the NHMRC.

The possibilities and opportunities in medical research are many and varied. MIMR's two-way street is a winding one, that will no doubt have its share of detours, but the outcomes, in terms of research, discovery and innovation in translational medicine, are well within our sights.

Bryan Williams
Institute Director



Chairman's Message

The opportunity to be involved in medical research in any small way is a privilege. As a Board Member, I cannot boast of discoveries at the laboratory bench, or publications in a high-ranking scientific journal, but it is an honour for me and my fellow Board Members to assist the Institute by sharing our skills and experience with such an outstanding team of medical researchers.

Throughout 2008, a key strategic focus was the integration and consolidation of resources and research across MIMR, Monash University and the Monash Health Research Precinct (MHRP). The MHRP incorporates research and clinical trials undertaken by scientists and clinicians at MIMR, Prince Henry's Institute, Southern Health and Monash University.

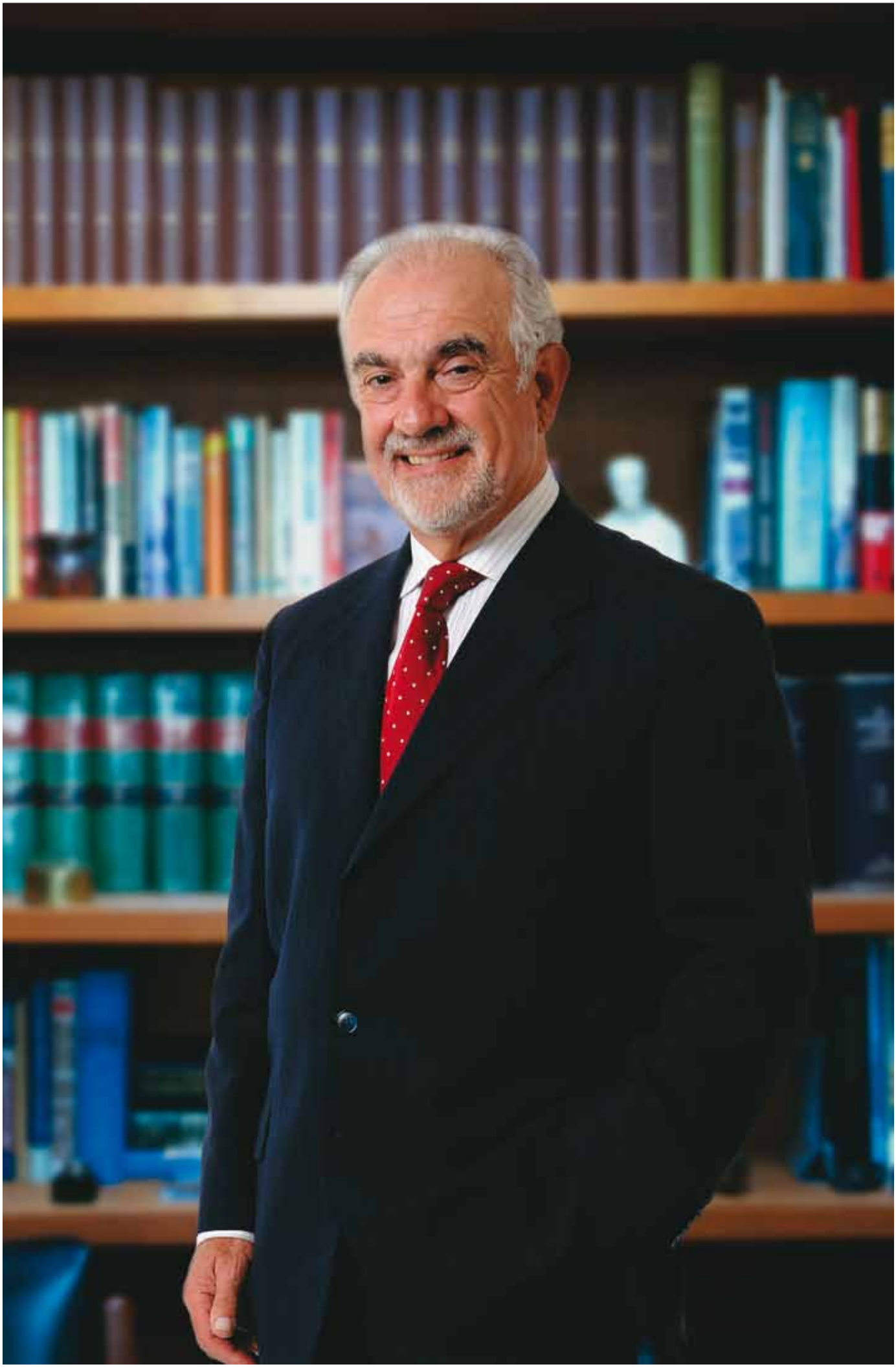
The MHRP translational research program remains a major focus of our efforts to bring together the basic research activities in our laboratories with patient care at the Monash Medical Centre. However, our ability to enhance these activities is hampered by space constraints. Consultation with Monash University and Southern Health to progress construction of an additional building to house Precinct researchers is ongoing. Despite there being no additional funding announced in the 2008-09 State Budget, we are optimistic that our ongoing relationship with the Department of Industry, Innovation and Regional Development will ensure a positive outcome for the Institute in the future.

A key project in 2008 was to start to map the ever-expanding cancer research undertaken at Monash University and MHRP. By identifying the type of cancer research taking place, and by which Chief Investigators, the University can ensure adequate allocation of funding and resources. In addition, it will allow greater collaboration and sharing of knowledge and skills by all scientists involved in this key area of medical research.

Early in the year, a report was sent to the National Hospitals and Health Reform Commission (NHHC), noting that the move away from research, development and education in Australia's hospitals is harmful. In May, a report from the NHHC was received which noted the importance of absorbing, implementing and creating new knowledge from clinical research, and that health technology is an exploding revolution which is needed as a continuum of education and training. Given the importance of collaboration and translational research for all MIMR scientists, this is a key issue we will closely monitor throughout 2009.

Medical research is dependent on the support, talents and dedication of all people involved. I would like to thank all Board Members, scientists, staff, students and our many individual and corporate supporters for their ongoing investment in MIMR's future. There will be many challenges to face in 2009 and beyond, but I know MIMR will continue to go from strength to strength.

George Pappas
Chair, Advisory Board



Governance

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

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Advisory Board Member for Australia and New Zealand, Oracle Corporation

National Deputy President, Australian Industry Group

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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

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

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CEO, Taxpayers Australia

Mr Andrew Evans

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

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Vice Chairman, Goldman Sachs JBWere Pty Ltd and Managing Director and Co-Chairman, Investment Banking Division

Member, Australian Government Takeovers Panel

Chairman, Burnet Institute

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Head, School of Biomedical Sciences, Monash University

Member, Victorian State Government Science and Biotechnology Advisory Committee

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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

Professor David Pennington AC

Company Director

Chairman, Bio21 Australia Ltd

Principal, Foursight Associates Pty Ltd

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

Professor Ian Smith

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

Director, Monash Biomedical Proteomics Facility

Chairman, National Health and Medical Research Council Grant Review Panel, Biochemistry

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

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

Mr Colin Wise

Non-executive Chairman, St Barbara Ltd

Chairman, St Barbara Ltd Remuneration Committee

Non-executive Director, Southern Health

Chairman, Southern Health Quality Committee

Fellow, Australian Institute of Company Directors

Fellow, Australasian Institute of Mining and Metallurgy

Professor Steve Wesselingh

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

Director, Burnet Institute 2002-2007

Director, Infectious Diseases, Alfred Hospital, 1999-2002

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 & Centre Director: Professor Bryan Williams

Senior Scientists: Prof Neil Watkins, Assoc Prof Greg Hannigan, Assoc Prof Terry Johns, 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. The Cancer Research team also collaborates closely with scientists from other Centres in MIMR and the Monash Health Research Precinct. Expertise, resources and knowledge are shared for research into a range of cancers, including breast, bladder, endometrial, ovarian, stomach, head and neck, kidney, and prostate cancers, as well as leukaemia.

The Centre for Cancer Research changed dramatically during 2008, with the arrival of Professor Neil Watkins and Associate Professors Greg Hannigan and Terry Johns. The recruitment of new staff and students has resulted in a doubling of the size of the Centre. This expansion has provided a stimulating and dynamic environment in which to work.

In November, the Centre organised the inaugural Monash Cancer Network Symposium. The Symposium was hosted by MIMR and was jointly sponsored by Southern Melbourne Integrated Cancer Services (SMICS). Cancer scientists from Monash University, MIMR, Prince Henry's Institute and Southern Health presented their latest research. Presentations were also made by BioGrid Australia, SMICS, the Victorian Cancer Biobank and the Victorian Cancer Agency.

Professor Bryan Williams was part of a collaboration that received the 2008 Boltzmann Award, an award established to encourage international scientific cooperation in the field of cytokines. Professor Ganes Sen (Lerner Research Institute, Cleveland Clinic) was the co-recipient of the award. Professors Williams and Sen shared the award with their postdoctoral fellows, Dr Saurabh Chattopadhyay (Lerner Research Institute, Cleveland Clinic) and Dr Joao Marques (Northwestern University, Chicago).

Dr Elizabeth Williams' research with Dr Renea Taylor (Centre for Urological Research) into the genes involved in the suppression of androgen-independent prostate cancer was selected as the inaugural MIMR Flagship Project. It is hoped their research will ultimately lead to the development of new treatments for this aggressive form of prostate cancer.

The Centre was very successful in obtaining funding throughout the year. Professor Neil Watkins was awarded an NHMRC Senior Research Fellowship, to commence in 2009. He was also awarded over $1.2 million in grants from the NHMRC, including two project grants as sole investigator, and a third project grant in collaboration with the Garvan Institute of Medical Research.

Associate Professor Terry Johns received a grant of US$386,500 from the James S McDonnell Foundation for his research to develop an effective targeted therapy to treat glioma, a malignant tumour of the brain. He also received US$243,120 from Amgen Inc. for further investigation into specific molecules involved in the development of glioblastomas.

One of the Centre's newest postdoctoral scientists, Dr Steve Greenall, received the inaugural Ron Evans Cancer Research Fellowship, which was set up in honour of the late Ron Evans AM. Dr Greenall is investigating the role that the protein c-met plays in the development and progression of cancer.

PhD student Matthew Thompson was awarded the Australian Rotary Health Research Fund/Rotary District 9650 Bowelscan Scholarship for his research into bowel cancer.

Research highlights

TLR7 is involved in sequence-specific sensing of single-stranded RNAs in human macrophages

This research uncovered an important aspect of innate immune sensing that had not been previously appreciated. A cell culture system was established that was able to replicate sensing of immunostimulatory RNA oligonucleotides by human white blood cells. The study showed that modulation of the relative expression ratio of human Toll-like receptor 7 (hTLR7) to hTLR8 in THP-1 monocytic cells correlated with differential sensing of immunostimulatory sequences. Suppression of hTLR7 expression by RNA interference in this model reduced sensing of all immunostimulatory single-stranded RNAs tested.

Not only did this establish for the first time that hTLR7 is involved in sequence-specific sensing of single-stranded RNAs, the results also suggested that differential sequence-specific sensing of RNA oligonucleotides could be the result of modulation of TLR7 sensing by human TLR8. Subsequent work currently being prepared for publication supports this notion.

Gantier MP, Tong S, Behlke MA, Xu D, Phipps S, Foster PS, Williams BRG (2008) TLR7 is involved in sequence-specific sensing of single-stranded RNAs in human macrophages. *J Immunol* 180:2117-2124.

Ets2 maintains hTERT gene expression and breast cancer cell proliferation by interacting with c-Myc

The gene human telomerase reverse transcriptase (hTERT) plays an important role in the immortality of cancer cells. This study examined the role of the transcription factor Ets2 in the expression of the hTERT gene and the proliferation of breast cancer cells.

It was found that silencing of the Ets2 gene resulted in a decrease in the expression of the hTERT gene in breast cancer cells, as well as an increase in apoptosis, or cell death. Apoptosis in these cells could be rescued by reconstitution with recombinant hTERT. Ets2 was shown to bind to the hTERT gene at two sites in the gene promoter, namely EtsA and EtsB. Mutation of either of the sites caused a reduction in the activity of the hTERT gene promoter.

c-Myc, a transcription factor of the hTERT gene, binds to the E-box on the gene promoter. Here, Ets2 was shown to form a complex with c-Myc. Binding of c-Myc to the E-box could be disabled by immunological depletion of Ets2 or mutation of the EtsA site of the hTERT gene. Moreover, the removal of c-Myc or mutation of the E-box reduced the binding of Ets2 to the EtsA site.

Thus the interactions between Ets2, c-Myc and the hTERT gene promoter play an important role in the expression of the hTERT gene, and the proliferation of breast cancer cells. This mechanism may be important for the development of new anti-cancer drugs.

Xu D, Dwyer J, Li H, Duan W, Liu J-P (2008) Ets2 maintains hTERT gene expression and breast cancer cell proliferation by interacting with c-Myc. *J Biol Chem* 283:23567-23580.

L to R: Prof Bryan Williams, Assoc Prof Terry Johns, Dr Elizabeth Williams, Assoc Prof Greg Hannigan, Prof Neil Watkins

Commercialisation

Australian Provisional Patent Application (AU2008900689), *Immunostimulatory molecules* (BRG Williams, MP Gantier and S Tong).

Provisional Patent Application (61/101/971), *Methods for the treatment of cancer* (TJ Johns).

Australian Provisional Patent Application (30512790), *A novel anti-inflammatory target to treat obesity-induced insulin resistance*, filed with MA Febbraio and GI Lancaster from the Baker IDI Heart and Diabetes Institute (BRG Williams and AJ Sadler).

Grants awarded in 2008

NHMRC Research Fellowship

DN Watkins
Research Fellowship Level B, 2009-2013

NHMRC Project Grants

DN Watkins
An in-vivo model of acquired chemoresistance in small cell lung cancer (2009-2011)
$349,500

DN Watkins
Interactions between hedgehog and Ras signalling in lung adenocarcinoma (2009-2011)
$284,250

A Swarbrick, DN Watkins, S O'Toole
The role of the hedgehog pathway in breast cancer (2009-2011)
$576,000

Victorian Cancer Agency Platform Technology Capacity Building Grant

ED Williams, DN Watkins, TG Johns, GE Hannigan, CE Gargett, ID Davis
Development of a high content screening platform for individualised cancer chemotherapy (2008)
$148,477

Contract Grants

TG Johns
Duel targeting of the EGFRvIII and c-met tyrosine kinase receptors in glioblastoma (2008-2010)
Amgen Inc, USD $243,120

BRG Williams
Protein-RNA recognition in innate immunity (2008-2009)
Roche Kulmbach GmbH, $220,000

ED Williams
Evaluation of VEGG/VEGFR family member expression levels in prostate, bladder and melanoma tumor cell lines and archival human tissue (2008-2010)
Vegenics Limited, $623,750

ED Williams
Efficacy of ZD0530 / AZD4054 combination in inhibiting metastasis (2008-2009)
Astra Zeneca United Kingdom Limited, $250,000

Philanthropic Grants

TG Johns
Establishing efficacious combinations of targeted therapies for the treatment of glioma (2008-2010)
James S McDonnell Foundation, USD $386,500

S Tong
Free fetal RNA in the maternal circulation: upregulation of hypoxic response genes during labour as a marker of fetal distress (2008)
The Sylvia and Charles Viertel Charitable Foundation: Clinical Investigator Grant, $60,000

BRG Williams
Advancing cancer research at MIMR (2008)
The Victor Smorgon Charitable Foundation, $30,000

ED Williams
Upright fluorescent microscope
Perpetual (Percy Baxter Charitable Trust), $72,958

MIMR Flagship Project Grant

R Taylor, ED Williams
Identification of genes involved in the suppression of the development of castrate-resistant prostate cancer (2009)
Monash Institute of Medical Research, $100,000

Scholarships, awards and promotions

Tung-Liang Chung
- International Society for Stem Cell Research Travel Award
- Australian Society for Stem Cell Research Conference Award

Dr Steve Greenall
- Ron Evans Cancer Research Fellowship, 2008-2010

Georgina Ryland
- APA (Australian Postgraduate Award) Scholarship
- First Class Honours, Monash University Faculty of Medicine, Nursing and Health Sciences
- Monash Jubilee Honours Scholarship - awarded to only the two highest achieving students
- Faculty Postgraduate Excellence Award
- Shortlisted for 2009 Australian Academy of Science – National Institutes of Health (NIH, USA) Visting Scientist Award

Rina Mohd Said
- Ministry of Higher Education Malaysia Scholarship

Matthew Thompson
- Australian Rotary Health Research Fund - Rotary District 9650 Bowelscan Scholarship, 2008-2009
  $25,000

Centre for Innate Immunity & Infectious Diseases

Centre Director: Professor Paul Hertzog

Senior Scientists: Dr Brendan Jenkins, Dr Ashley Mansell

Formerly the Centre for Functional Genomics and Human Disease, the Centre underwent a name change in 2008 to reflect an evolution in research focus.

The newly-named Centre for Innate Immunity and Infectious Diseases (CIIID) focuses on the molecular regulation of the innate immune response. This early immune response determines how the body responds to infections by pathogens. It initiates the inflammatory response and can modulate the development of cancers. By understanding the molecular pathways that regulate these processes as well as their normal, physiological roles, CIIID scientists aim to contribute to the development of new approaches to the prevention, diagnosis and treatment of disease using drugs and prevention vaccines.

Scientists in CIIID have formed an international collaboration between with the University of Manitoba in Canada, which was formalised in early 2008. The research program received a $600,000 grant from the Victorian and Manitoban Governments to use novel gene targeted mouse models for new approaches to study the role of the immune system in cancer development and progression. Professor Paul Hertzog and Dr Brendan Jenkins, two of the collaboration's principal investigators, will use their expertise in the role inflammatory diseases can play in the onset of cancer, such as the links between hepatitis and liver cancer, and gastritis and gastric (stomach) cancer.

The Cooperative Research Centre for Chronic Inflammatory Diseases (CRC-CID), a Federal Government initiative of which CIIID was a key partner, ended in June 2008. The research will continue with collaborative and commercial partners in the future. As part of the CRC-CID program, Professor Paul Hertzog and Dr Ashley Mansell coordinated the Innate Immune Sculpting of Adaptive Immunity conference at Hamilton Island in April, which was attended by 100 national and international attendees.

Dr Brendan Jenkins was part of a collaborative study that discovered the signalling pathway of the Stat3 protein inside stomach cells could prevent inflammation and tumour formation in pre-clinical models of gastric cancer. In addition to providing a greater understanding of how stomach cancer develops, this groundbreaking finding could also lead to the identification of potential markers that may help in the early detection of gastric cancer.

Dr Jenkins' research received a further boost when he was named one of only two Australian scientists to receive the Sylvia and Charles Viertel Charitable Foundation Senior Medical Research Fellowship. This five-year, million dollar grant will enable him to expand his research into the role of cytokine signalling pathways in the molecular pathogenesis of inflammation and cancer. Dr Jenkins was also awarded a Young Tall Poppy Award from the Australian Institute for Policy and Science, which recognises high achievers with an outstanding professional and personal commitment to scientific research in Victoria.

CIIID was pleased to welcome new Research Fellows; Dr Alexander Drew and Dr Niamh Mangan. Dr Shamith Samarajiwa left MIMR to take up an appointment at the Cambridge Research Institute of Cancer Research, UK to continue his research in bioinformatics. The Centre also farewelled Dr Bernadette Scott after 12 years of service.

Research highlights

STAT3 and STAT1 mediate IL-11-dependent and inflammation-associated gastric tumorigenesis in gp130 receptor mutant mice

A common feature of many human cancers, including gastric (stomach) cancer is deregulated activation of the latent signal transducer and activator of transcription (Stat)3 transcription factor. It is well established that increased Stat3 activation promotes an anti-apoptotic, pro-angiogenic and pro-proliferative environment for neoplastic cells. However, the molecular mechanisms leading to deregulated Stat3 activation in cancer remain ill defined. This research has utilised a unique mouse model (*gp130*$^{F/F}$) for chronic gastric inflammation and tumourigenesis to uncover that interleukin (IL)-11 promotes gastric disease. At the molecular level, these mice are characterised by elevated Stat3 and Stat1 activation as a consequence of the inability of the negative regulator suppressor of cytokine signalling (Socs)3 to bind to the mutated gp130 signalling receptor subunit. Specifically, genetic deletion of the IL-11 ligand-binding receptor subunit in *gp130*$^{F/F}$*:IL-11Rα*$^{-/-}$ mice completely prevented the onset of gastric disease and coincided with normalised gastric Stat3 activation and IL-11 expression. Furthermore, reducing Stat3 activity in gp130F/F mice, either genetically or by therapeutic administration of Stat3 antisense-oligonucleotides, normalised gastric IL-11 expression and suppressed tumourigenesis. Notably, genetically reducing the activity of Stat1 in *gp130*$^{F/F}$ mice also reduced gastric inflammation and tumourigenesis, and coincided with reduced gastric IL-11 expression.

Taken together, this research reveals for the first time that IL-11 is the key cytokine that triggers excessive activation of Stat3 and Stat1 in the stomach, which in turn leads to chronic inflammation and tumourigenesis.

Ernst M, Najdovska M, Grail D, Lundgren-May T, Buchert M, Tye H, Matthews VB, Armes J, Bhathal PS, Hughes NR, Marcusson EG, Karras JG, Na S, Sedgwick JD, Hertzog PJ, Jenkins BJ (2008) STAT3 and STAT1 mediate IL-11-dependent and inflammation-associated gastric tumorigenesis in gp130 receptor mutant mice. *J Clin Invest* 118:1727-1738.

A conserved IFN-alpha receptor tyrosine motif directs the biological response to type

Interferons are key proteins that regulate the immune response to infection and cancer. However, if unchecked, interferon signalling can form the basis of inflammatory disease. This study discovered key points of the interferon receptors that transmit these signals and may form potential targets to block dangerous IFX signalling.

Zhao W, Lee C, Piganis R, Plumlee C, de Weerd N, Hertzog PJ, Schindler C (2008) A conserved IFN-alpha receptor tyrosine motif directs the biological response to type I IFNs. *J Immunol* 180:5483-5489.

Grants awarded in 2008

Victorian Department of Innovation, Industry & Regional Development (DIIRD) Grant

P Hertzog, B Jenkins
MONMAN initiative - mouse modelling in human disease (2008-2009)
Victorian Government Support Funding – Australian-Canadian Initiative, $200,000

Philanthropic Grants

B Jenkins
The role of cytokine signalling pathways in the molecular pathogenesis of inflammation and cancer (2009-2013)
The Sylvia and Charles Viertel Charitable Foundation: Senior Medical Research Fellowship, $975,000

Association for International Cancer Research Grant

B Jenkins, A Mansell, R Ferrero
Cross-talk between cytokine and pathogen recognition receptor networks in the pathogensis of gastric cancer (2009-2011)
GBP£162,950

Scholarships, awards and promotions

Dr Brendan Jenkins

- Monash University Faculty of Medicine, Nursing and Health Sciences Travel Award
- International Society for Interferon and Cytokine Research Travel Award, Cytokines 2008 Conference, Montreal, Canada
- Victorian Tall Poppy Award for Medical Research Excellence

L to R: Dr Brendan Jenkins, Dr Ashley Mansell, Prof Paul Hertzog

Centre for Pain Medicine & Palliative Care

Centre Director: Professor Colin Goodchild

The Centre is the focus for research in the field of pain medicine, including palliative care. The core ongoing activity concerns research into drugs, given alone and in combinations, to maximise pain relief efficacy while minimising side effects common with these drugs. This core activity encompasses a commercial relationship with CNSBio, a Monash University spin-out company. The Centre collaborates with scientists and clinicians in other Centres and departments to perform preclinical and clinical research. Professor Goodchild teaches at undergraduate and postgraduate level and also heads the Pain Medicine Outpatients Clinic at Southern Health.

In 2008, a new pain model was developed at the Centre. This is the first rat model of prostate bone cancer pain in Australia and one of only three in the world. The model was used successfully in a project showing potentiation of the antinociceptive effects of morphine by concurrent administration of the KCNQ2-3 potassium channel modulator, flupirtine. These results were presented as a poster in November at the Australian Health and Medical Research Congress in Brisbane.

Prof Colin Goodchild

Commercialisation

The Centre continues its collaboration with CNSBio. Three new patents were filed arising from the work performed in the laboratory.

Professor Goodchild, in his role as Chief Scientific Officer at CNSBio, has helped design and implement a Phase 2 trial of CNSB001 (flupirtine) in the treatment of HIV-associated neuropathic pain. This is being conducted by clinicians at the Alfred Hospital in Melbourne and at hospitals in Sydney. He has also been involved with the trial design of a Phase 2b study of the same drug to be conducted on patients with painful diabetic neuropathy in Germany.

New patent applications

Provisional Patent Application, on the use of CNSB004 (leconotide) in treatment of neuropathic and inflammatory pain, filed in 2008

Provisional Patent Application (30599578), on the use of CNSB002 in treatment of neuropathic and inflammatory pain, filed in 2008

A Patent Cooperation Treaty patent application (PCT no 30571160), on the use of neurokinin 1 antagonists in treatment of neuropathic pain, filed in 2008

Centre for Reproduction & Development

Centre Director: Professor Michael Holland

Deputy Centre Director: Associate Professor Mark Hedger

Senior Scientists: Assoc Prof Kate Loveland, Assoc Prof Moira O'Bryan, Assoc Prof David Phillips, Dr Ursula Manuelpillai, Dr Paul Verma

The Centre for Reproduction and Development (CRD) applies knowledge gained from the study of mammalian development and reproductive biology, to develop solutions to practical problems in medicine and biotechnology. The major focus of the Centre's research is male reproductive function, principally testis biology and immunology, infertility and contraception, and assisted reproductive technologies, which include stem cell research and cloning. This diverse base has allowed CRD to contribute to basic and translational research, in both medical and animal biotechnology.

The Centre received ongoing, strong support from both traditional grant schemes, such as the ARC and NHMRC, and commercial schemes and companies including the Dairy CRC, Genetics Australia, Viagen and BayerSchering Pharma AG.

Throughout 2008 the Centre's research program continued to expand. Two new NHMRC Grants were awarded, funding support from the Victorian State Government and industry was also received. While 2008 saw the end of the Dairy CRC, an application for a renewal of this CRC will be lodged in 2009. The ARC Centre of Excellence in Biotechnology and Development continued to provide $850,000 annually to the Centre. These grants, plus existing grants, provide a strong future for CRD.

Stem cell research is an expanding area within the Centre. In 2008, Dr Ursula Manuelpillai and her research group from the Centre for Women's Health Research join CRD. Dr Manuelpillai's interests in adult stem cells isolated from the amnion mesh well with Dr Paul Verma's interests in embryonic stem cells and induced pluripotent stem-like (iPS) cells.

Dr Verma's iPS cell research received significant support from the Victorian Government in September. The Victorian Minister for Innovation, Gavin Jennings, visited MIMR to announce a joint $455,450 grant for a collaborative stem cell research project between Dr Verma and a New South Wales research team funded by the New South Wales Government. The funding has allowed Dr Verma to create Australia's first iPS cells; a breakthrough of international significance.

L to R: Dr Ursula Manuelpillai, Assoc Prof Mark Hedger, Assoc Prof Kate Loveland, Prof Michael Holland, Dr Paul Verma, Assoc Prof Moira O'Bryan, Assoc Prof David Phillips

The stem cell research program also received support through Monash University's International Program. This funding has provided the opportunity to collaborate with Professor Justin St John's group at the University of Warwick, United Kingdom. As part of this collaborative project, Professor St John visited MIMR in early 2008 to spend a two-month period in CRD, funded by an Endeavour Senior Scientist Award.

CRD scientists continued to receive accolades for their research. The promotion of Associate Professors Moira O'Bryan and Kate Loveland to NHMRC Senior Research Fellows was well deserved. Associate Professor O'Bryan received the Young Andrologist Award from the American Society of Andrology, recognising her contribution to male reproduction. It was encouraging to see some of the Centre's up-and-coming young scientists and students win travel awards.

An important facet of the Centre is its Education Program in Reproduction and Development, which conducts two Masters programs: Clinical Embryology and Reproductive Science. These programs give students the skills to work in IVF clinics and the opportunity to broaden their skills in animal biotechnology.

Our publication record continued to improve, with nearly 40 peer-reviewed papers published in 2008. In addition, eight students successfully completed their PhDs, two completed Masters degrees and three undertook an Honours year.

Research highlights

Mitochondrial DNA transmission and transcription after somatic cell fusion to one or more cytoplasts

Cloned embryos contain mitochondrial DNA from both the donor cell and recipient oocyte. To test whether the genetic divergence between donor cell and recipient cytoplast mitochondrial DNA influences development, cloned bovine embryos were created by fusing a donor cell with one or more cytoplasts. Analysis of the mitochondrial DNA showed that embryos made with either two or three cytoplasts had significantly more mitochondrial DNA variance than did fetal tissue. Phylogenic analysis of embryos made with single cytoplasts showed three distinct groups with varying genetic divergence from the donor cell line. The degree of evolutionary distance between donor cell and cytoplast, and the variability in heteroplasmy between different tissues, has implications for divergent intergeneric nuclear transfer and production of embryonic stem cells.

Bowles EJ, Tecirlioglu RT, French AJ, Holland MK, St John JC (2008) Mitochondrial DNA transmission and transcription after somatic cell fusion to one or more cytoplasts. *Stem Cells* 26:775-782.

Genome analysis of the platypus reveals unique signatures of evolution

The platypus (*Ornithorhynchus anatinus*) is a unique and important part of Australia's native fauna and has, since its discovery by science in the late 18th century, provoked fascination and controversy, particularly about its evolutionary relationships.

In 2004 a group of scientists from Australia and the US began planning a project to sequence the genome of the platypus. In 2008 the results of the efforts of 104 scientists, from 33 different institutions and nine countries, were published in *Nature*.

The genome sequence has confirmed that the platypus shares many features with the genome sequences of mammals, birds and reptiles and has revealed new clues as to how mammals evolved. For example, reptile and platypus venom proteins have evolved independently from the same gene families; expansions in the families of immune genes are directly related to platypus biology, and milk protein genes are conserved despite platypuses laying eggs. Platypus milk proteins form a cluster that matches those of humans, suggesting that one of the genetic innovations that led to the development of milk occurred more than 166 million years ago, after mammals first split from the lizard-like sauropsid reptiles that gave rise to modern reptiles and birds.

The platypus now faces perhaps the greatest challenge in its long evolutionary history: a 'perfect storm' of climate change, habitat loss, environmental pollution and the possible introduction of diseases spread via global trade and transport. Sequencing of the platypus genome provides a valuable resource for comparative analyses, for exploring at the molecular level the unique facets of its biology, and for future conservation strategies.

Warren WC, Hillier LW, Marshall Graves JA, Birney E, Ponting CP, Grutzner F, Belov K, Miller W, Clarke L, Chinwalla AT, Yang SP, Heger A, Locke DP, Miethke P, Waters PD, Veyrunes F, Fulton L, Fulton B, Graves T, Wallis J, Puente XS, Lopez-Otin C, Ordonez GR, Eichler EE, Chen L, Cheng Z, Deakin JE, Alsop A, Thompson K, Kirby P, Papenfuss AT, Wakefield MJ, Olender T, Lancet D, Huttley GA, Smit AF, Pask A, Temple-Smith P, et al (2008) Genome analysis of the platypus reveals unique signatures of evolution. *Nature* 453:175-183.

Commercialisation

The closure of the Dairy CRC in mid-2008 saw a number of patents returned to Monash. One of these involves a new, generally applicable method for isolation of embryonic stem cells. We have recently used this patent to develop a commercial relationship with American animal biotechnology company, Viagen to explore the use of our research findings to repair tendon and joint damage in horses.

Grants awarded in 2008

NHMRC Research Fellowships

K Loveland
Research Fellowship Level B, 2009-2013

M O'Bryan
Research Fellowship Level B, 2009-2013

NHMRC Project Grants

K Loveland, M Hedger, S Meacham
Activin in testicular development and disease (2009-2011)
$491,250

B Nixon, E McLaughlin, M O'Bryan
Human sperm-oocyte interaction (2009-2011)
$474,000

Australian Research Council / Centre of Excellence

J Aitken, G Hime, M Holland, D Jans, P Koopman, K Loveland, E McLaughlin, M O'Bryan, A Sinclair, S Roman
Biotechnology and development (2008-2010)
$6.4 million

Victorian Department of Innovation, Industry & Regional Development (DIIRD) Somatic Cell Nuclear Transfer Research Grant

P Verma, V Hall, N Richings
Generation of patient specific pluripotent stem cell lines by somatic cell reprogramming (2008-2010)
$205,450 – DIIRD contribution (total grant: $455,450)

Contract Grant

P Verma
Examine feasibility of isolating embryonic stem (ES) cells from horse embryos and investigate differentiation potential of such ES cells (2008-2009)
Viagen Inc Contract Grant, $158,500

Philanthropic Grants

D Phillips
Activin: can it help with cancer diagnosis and treatment? (2008)
Rotary Club of Balwyn, $27,500

P Temple-Smith
Control and management of fibrosis and fibrotic disease models (2008-2010)
Advanced Plastic Surgery Education Foundation, $55,000

Scholarships, awards and promotions

Dr Claire Borg
- Society for the Study of Reproduction (USA) Travel Award

Dr Nancy D' Cruz
- Australian Federal Government Department of Agriculture, Fisheries and Forestry, Young Innovator and Scientist Award

Dr Gerard Gibbs
- CASS Foundation Travel Award

Assoc Prof Mark Hedger
- Appointed President-elect, Society for Reproductive Biology (2008-2009)
- NHMRC 10 of the Best Research Projects 2008

Dr Cathryn Hogarth
- Monash University Vice Chancellor Commendation for Doctoral Thesis in 2007

Dr Duangporn Jamsai
- International Society of Andrology Travel Award
- Outstanding Trainee Investigator Award, American Society of Andrology
- CASS Foundation Travel Award

Assoc Prof Moira O' Bryan
- Young Andrologist of the Year, American Society of Andrology

Assoc Prof David Phillips
- Australian Academy of Science, Scientific Visits to Europe Travel Award

Dr Katja Wolski
- Lonnie D Russell Travel Award, American Society of Andrology
- Ian Potter Foundation Travel Grant

Ritchie Centre for Baby Health Research

Acting Centre Director: Dr Philip Berger

Scientific Director: Associate Professor Rosemary Horne

Clinical Director: Dr Andrew Ramsden, Director, Monash Newborn

Senior Scientist: Dr Gillian Nixon

The Ritchie Centre for Baby Health Research has established an international reputation for excellence in fetal, newborn, neonatal and paediatric research. 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 productivity of the Centre is built upon state-of-the-art animal and human laboratories and ready access to patients under clinical care in Southern Health.

During the course of 2008, newly appointed consultants in Monash Newborn, Southern Health have brought high level skills to the Centre. Dr Alex Veldman specialises in the molecular biology of inflammation and coagulation, two processes that underpin chronic lung disease, which is a major cause of mortality and morbidity in the preterm infant. Dr Arvind Sehgal has brought his experience in the circulatory problems of infants with persistent ductus arteriosus to the Ritchie Centre. This condition can lead to fatal diseases of the newborn, such as necrotising enterocolitis and brain injury.

Babies and children will be the primary beneficiaries of new, state-of-the-art, sleep monitoring facilities opened in August 2008 at the Melbourne Children's Sleep Unit, Monash Medical Centre; Victoria's only paediatric sleep unit. The facility, jointly funded by the Ritchie Centre and the Melbourne Children's Sleep Unit, is devoted to clinical and research sleep studies. A key goal for the new facility is to improve understanding of how the known risk factors for Sudden Infant Death Syndrome (SIDS), such as sleeping infants on their tummies and smoking during pregnancy, lead to the death of babies.

In October, the Ritchie Centre announced the appointment of Dr Mandar Joshi as the inaugural Victor Y-H Yu Fellow. Dr Joshi undertook his PhD in Columbus Ohio, USA in 2005. The Victor Y-H Yu Fellowship was established by a generous donation from the Reverend Professor Victor Y-H Yu AM in 2007. The aims of the Victor Y-H Yu Fellowship are to attract outstanding graduates to the area of perinatal and paediatric health research; to enhance the research and intellectual skills of early career clinicians and scientists wishing to make research a key element of their careers, and to encourage the rapid translation of research into clinical practice.

At the end of 2008, the Centre announced the creation of WI McNab Scholarships, in memory of Wilhelmina McNab whose estate was passed to the Ritchie Centre in 2008. The Scholarships will be offered to suitably qualified University graduates to pursue postgraduate research in the Ritchie Centre in areas relating to the growth, health and well-being of babies, infants and children. The first WI McNab Scholars will be announced in 2009.

The annual Kaarene Fitzgerald Lecture was hosted by the Ritchie Centre in November 2008. The lecture honours Kaarene Fitzgerald AC, founder of the Sudden Infant Death Research Foundation. The 2008 Kaarene Fitzgerald Lecture was entitled *Update on Causes of Neonatal Death*. Associate Professor Rosemary Horne, Scientific Director, Ritchie Centre, presented *Safe Sleep in 2008 – New Controversies* and Professor Euan Wallace, Clinical Director, Centre for Women's Health Research, discussed *New Horizons in Still Birth and Preterm Labour.*

Research highlights

Increased peripheral chemosensitivity via dopaminergic manipulation promotes respiratory instability in lambs

Periodic breathing (PB), which is characterised by clusters of breaths separated by intervals of apnea or reduced ventilation, is commonly observed in preterm human infants as well in adult subjects at altitude, and in patients with idiopathic central sleep apnea or heart failure. In the preterm infant, PB can be associated with rapid and profound arterial desaturation, prolonged apnea and cerebral deoxygenation. This suggests that it could play a role in the cardio-respiratory and brain pathologies that commonly accompany prematurity.

To examine the causes of this respiratory pattern, domperidone, a dopamine D(2)-receptor antagonist, was used to increase the sensitivity of the carotid body to O_2 and CO_2. The hypothesis was that heightened chemoreceptor sensitivity would promote PB through an increase in the loop gain (LG) of the respiratory control system.

Domperidone significantly increased controller gain for oxygen and increased the incidence and epoch duration of PB. Domperidone also decreased the duty ratio PB, which is the ratio of the ventilatory phase of the PB cycle divided by the total cycle duration. These changes are consistent with domperidone increasing LG. Although domperidone increased controller gain for CO_2, the contribution of CO_2 oscillations to the genesis of PB in the lamb remained small.

It was concluded that domperidone increases LG in the lamb via an increase in controller gain for O_2. Our study demonstrates that a quantitative understanding of the factors that determine LG provides insight into the cause of PB.

Edwards BA, Sands SA, Skuza EM, Stockx EM, Brodecky V, Wilkinson MH, Berger PJ (2008) Increased peripheral chemosensitivity via dopaminergic manipulation promotes respiratory instability in lambs. *Respir Physiol Neurobiol* 164:419-428.

Blood pressure and heart rate patterns during sleep are altered in preterm-born infants: implications for sudden infant death syndrome

Preterm infants are at an increased risk of sudden infant death syndrome (SIDS), which may result from immature control of heart rate (HR) and blood pressure (BP). Previous studies demonstrate that preterm infants have altered HR and BP control at term-equivalent age; however little information is available beyond term-equivalent age. The aim of this study was to determine the effect of preterm birth on HR and BP control over the first six months of life after reaching term-equivalent age, including the age when SIDS risk is greatest, to understand the pathogenesis of SIDS.

Twenty-five preterm infants and twenty term infants were studied longitudinally at two-four weeks, two-three months and five-six months term-corrected age (CA) using daytime sleep studies (polysomnography). BP was measured with a small cuff placed around the infant's wrist during both quiet (QS) and active sleep (AS).

The study showed that BP was lower in the preterm group during both QS and AS at all ages studied ($p<0.05$). In contrast, there were no differences between groups in HR. Within the preterm group, BP averaged lower at two-three months CA compared to both two-four weeks and five-six months CA, and was lower in QS compared to AS at all ages studied ($p<0.05$). HR fell with increasing age, and was lower in QS compared to AS at five-six months CA ($p<0.05$).

This study found that sleep state and age affect HR and BP patterns in prematurely born infants over the first six months of term-corrected age. Notably, preterm infants had persistently lower BP compared to age-matched term infants, signifying long-term alterations in cardiovascular control in infants born prematurely.

Witcombe NB, Yiallourou SR, Walker AM, Horne RS (2008) Blood pressure and heart rate patterns during sleep are altered in preterm-born infants: implications for sudden infant death syndrome. *Pediatrics* 122:e1242-1248.

L to R: Assoc Prof Rosemary Horne, Dr Philip Berger, Dr Andrew Ramsden, Dr Gillian Nixon

Commercialisation

US patent (7,347,824), *Method and apparatus for determining conditions of biological tissues* (MH Wilkinson, CA Ramsden, PJ Berger).

US Patent (7,201,721), *Measuring tissue mobility* (MH Wilkinson).

Grants awarded in 2008

Philanthropic Grants

G Nixon
The impact of obstructive sleep apnea on cardiovascular function: are children with Down syndrome at higher risk? (2008)
Windermere Foundation, $14,879

CA Ramsden
Evaluating the potential of Protein C to modulate the inflammatory process in neonatal chronic lung injury (2008)
Windermere Foundation, $15,000

A Veldman, P Berger
Chronic lung disease in the preterm neonate: identifying therapies (2008)
Marian & EH Flack Trust, $30,000

F Wong
Novel approaches to bedside monitoring of cerebral oxygenation in infants with HIE undergoing therapeutic hypothermia (2008)
Kathleen Tinsley Clinical Research Fellowship, $47,000

Scholarships, awards and promotions

Priscila Cassaglia
- Harold Mitchell Foundation Postgraduate Travel Fellowship

Michele Hepponstall
- Best student poster presentation
- 3rd Annual Scientific Conference, Monash University Healthy Start to Life Network

Simon Hew
- New Investigator Award, Perinatal Society of Australia and New Zealand

Heidi Richardson
- International Society for the Study and Prevention of Infant Death Travel Award
- Second Prize, Fourth Year MIMR Postgraduate Student Symposium

Nicole Witcomb
- Perinatal Society of Australia and New Zealand New Investigator Award
- International Society for the Study and Prevention of Infant Death Travel Award
- First prize, Third Year MIMR Postgraduate Student Symposium

Dr Mandar Yoshi
- Victor Y-H Yu Fellowship

Centre for Urological Research

Centre Director: Professor Gail Risbridger

Clinical Director: Associate Professor Mark Frydenberg

Senior Scientist: Dr Renea Taylor

Scientists and clinicians working in the Centre for Urological Research (CURe) investigate the three clinical conditions that affect the prostate gland: prostate cancer, benign prostate hyperplasia (BPH) and prostatitis. These are all common conditions that have an immeasurable impact on quality of life for men and their families.

The Centre has close affiliations with universities, hospitals and other research institutes. To complement their prostate cancer research, CURe participates in a number of collaborations and consortia, including the Australian Prostate Cancer BioResource, the Victorian Prostate Cancer Research Collaboration, The Australian-Canadian Prostate Cancer Research Alliance, and Andrology Australia.

The CURe team's main areas of research interest are aligned with the contemporary issues in the field. Stem cell research is a key focus, as scientists aim to understand how prostate disease occurs through disrupted stem cell development and function.

Understanding the role and regulation of prostate stem cells is fundamental to developing new therapies for prostate cancer and BPH. Patient specimens are used to define how other cells in the tumour or overgrown tissue (from patients with BPH), tell the stem cells to 'behave badly', or how the microenvironment determines prostate stem cell behaviour. CURe's prostate stem cell research project leader, Dr Renea Taylor, has received international acclaim for her work. In 2008, Dr Taylor was awarded a Prostate Cancer Foundation of Australia (PCFA) Young Investigator Grant and the inaugural PCFA Rotary Research Fellowship that will provide funding for her research for the next four years.

The other main research focus within CURe is how reproductive hormones fuel prostate disease, with a view to developing hormone-based therapies. Hormones, in particular estrogens, are drivers in both prostate and breast cancer. Although they are more commonly associated with breast cancer, estrogens are also found in men and have been adversely and beneficially implicated in prostate disease and health. CURe scientists are involved in preclinical testing for the efficacy of β-selective estrogen receptor modulators for the treatment and prevention of BPH and prostate cancer, in an eight-year collaboration with BayerSchering Pharma AG. This productive partnership has provided $2.3 million to support this research program.

In 2008, CURe scientists and collaborators at the Monash Institute of Health Services Research conducted qualitative research in the community to analyse the effectiveness of different types of educational material on prostate cancer screening. Given the popular debate and controversies over screening for prostate cancer, this research evaluation is particularly valuable and informative for men with prostate cancer who are searching the internet for accurate, relevant information.

L to R: Prof Gail Risbridger, Dr Renea Taylor

Throughout 2008, philanthropic donations to CURe came from a variety of sources, including generous individuals and organisations. The Centre is indebted to Mr and Mrs George and Janet Limb, who have provided funding for two PhD scholarships through the Limb Family Foundation. Shirin Hussain and Sarah Wilkinson were awarded the scholarships at the beginning of their PhD studies in 2008. Significant support for the Centre's prostate cancer research program continued through the generosity of an anonymous donor.

Dr Kara Britt, a CJ Martin Fellow, returned to Melbourne from the Breakthrough Breast Cancer Research Centre at the Institute of Cancer Research in the UK joined CURe in 2008. Working on breast cancer stem cells, Dr Britt is investigating how hormones regulate the number of mammary stem cells and their differentiation, and the relationship to disease risk.

Research highlights

Minireview: regulation of prostatic stem cells by stromal niche in health and disease

The isolation and characterisation of prostatic stem cells has received significant attention in the last few years based on the belief that aberrant regulation of adult stem cells leads to prostate disease including cancer, although the nature of the perturbations in stem cell regulation remain poorly defined. Although adult stem cells can be governed by autonomous regulatory mechanisms, the stromal niche environment also provides essential cues to direct differentiation decisions and can lead to aberrant proliferation and/or differentiation. Previous studies have demonstrated that quiescent epithelial tissues containing adult stem cells are capable of altered differentiation in response to inductive and instructive mesenchyme. More recently, evidence suggests that embryonic mesenchyme is sufficiently powerful to direct the differentiation of embryonic stem cells into mature prostate or bladder. Additionally, prostatic tumour stroma provides another unique niche or microenvironment for stem cell differentiation that is distinct to normal stroma. In this review article, we highlight the importance of the appropriate selection of the stromal cell niche for tissue regeneration and implies plasticity of adult stem cells that is dictated by the tissue microenvironment.

Risbridger GP, Taylor RA (2008) Minireview: regulation of prostatic stem cells by stromal niche in health and disease. *Endocrinology* 149:4303-4306

Prostatic hormonal carcinogenesis is mediated by in situ estrogen production and estrogen receptor alpha signalling

Prostatic growth and function is primarily regulated by androgens such as testosterone, however testosterone by itself cannot cause prostate cancer (PCa). Previous studies have demonstrated that estrogens are able to regulate prostate growth, however two different estrogen receptors (ERα, ERβ) exist and appear to have opposing actions that may contribute to or prevent carcinogenesis. The aim of this study was to determine if local in situ production of estrogen affects prostatic carcinogenesis, and which estrogen receptor is involved in promoting carcinogenesis. Using a combination of testosterone and estradiol to induce prostate cancer in mice, we treated estrogen-deficient ArKO and wild-type mice and observed a reduced susceptibility to hormonal carcinogenesis in ArKO mice, implicating increased in situ estrogen production with increased risk of developing PCa.

Repeating this study in ERα knockout, and ERβ knockout mice, it was demonstrated that βERKO mice showed histological evidence of prostatic carcinogenesis similar to wild-type mice, but prostates of αERKO mice showed no evidence of carcinogenesis. These data demonstrate that antagonism of ERα activity may prevent prostatic carcinogenesis. Further, this mouse model of PCa may become a versatile model in which to examine genetic influences on prostate disease and to test therapeutics for PCa.

Ricke WA, McPherson SJ, Bianco JJ, Cunha GR, Wang Y, Risbridger GP (2008) Prostatic hormonal carcinogenesis is mediated by *in situ* estrogen production and estrogen receptor alpha signaling. *FASEB J* 22: 1512–1520.

Grants awarded in 2008

NHMRC Project Grant

G Risbridger
Characterising the beneficial effects of estrogen on the prostate gland (2009-2011)
$571,500

Australian Research Council Project Grant

G Risbridger, R Taylor
Keeping stem cells on track: maintaining organ and tissue homeostasis (2009-2010)
$307,000

Australian Research Council Linkage, Infrastructure, Equipment and Facilities Scheme

DJ Handelsman, RJ Norman, GP Risbridger, PY Liu
Liquid chromatography tandem mass spectrometry steroid analysis facility (2008)
$356,000

Cancer Council Victoria Project Grant

G Risbridger
Defining the relationships between estrogens, prostatitis and prostate cancer (2009-2011)
$300,000

Scholarships, awards and promotions

Dr Preetika Balanathan
- GlaxoSmithKline Australia Postdoctoral Award

Dr Stuart Ellem
- Aromatase Conference, Shanghai, China Travel Award

Shirin Hussain
- Limb Family Foundation PhD Scholarship

Dr Renea Taylor
- Prostate Cancer Foundation of Australia Rotary Research Fellowship
- Trainee Poster Prize Basic Science - Female Reproduction III category, The Endocrine Society's 90th Annual Meeting, San Francisco, USA

Sarah Wilkinson
- Limb Family Foundation PhD Scholarship

Centre for Women's Health Research

Centre Director: Professor Peter Rogers

Clinical Director: Professor Euan Wallace

Senior Scientists: Dr Caroline Gargett, Dr Jane Girling

The Centre for Women's Health Research undertakes clinical and fundamental research with the goal of providing better health outcomes for women. The Centre is strategically located within the Monash University Department of Obstetrics and Gynaecology and has an international reputation for facilitating interaction between clinicians and basic scientists.

The Centre has a wide-ranging research portfolio in applied and translational work on clinical problems such as endometriosis, pre-term birth, infertility and reproductive cancers, through to fundamental studies on biological processes such as angiogenesis, stem cell differentiation and synchrotron-generated x-rays.

In March, Professor David Healy, Chair, Monash University Department Obstetrics and Gynaecology, played a major role in hosting the 10th World Congress on Endometriosis in Melbourne. MIMR scientists' support of the conference included organisation of a one-day workshop that developed and published the first set of comprehensive research priority guidelines for endometriosis.

Throughout the year, staff and students received international recognition for their work with 16 different invited overseas seminars and lectures, and awards at the World Congress on Endometriosis and the Annual Meeting of the Society for Gynaecologic Investigation in San Diego, USA. Closer to home, Drs Caroline Gargett and Stephen Tong received awards from the NHMRC in recognition of their research accomplishments.

Monash University applied some of the funds generated through the sale of Monash IVF, a University company developed from research undertaken in the Department of Obstetrics and Gynaecology, to establish an endowed chair. Professor Euan Wallace, the Centre for Women's Health Clinical Director, was appointed the inaugural Carl Wood Endowed Chair in Obstetrics.

A number of new research scientists joined the Centre during the year: Drs Susie Millar, Carl Sprung, Tu'uhevaha Kaitu'u-Lino and Rebecca Lim.

In the second half of 2008, a major refurbishment of the Centre was undertaken with financial support from the Faculty of Medicine, Nursing and Health Sciences to provide new office space for the increased number of research staff. While this has lessened the short-term overcrowding problem, we remain committed to further expansion of the Women's Health Research Program with additional space in the planned new Monash Health Research Precinct building.

Research highlights

Identification of surface markers for prospective isolation of human endometrial stromal colony-forming cells

Dr Caroline Gargett and her team recently discovered a rare population of mesenchymal stem cells in human endometrium, the highly regenerative lining of the uterus, using retrospective stem cell assays. This paper reports on the screening of human endometrial stromal cells with potential stem cell markers to enable the prospective isolation of human endometrial stromal cells with colony-forming activity as a functional assay of adult stem cells. Of the four markers examined, it was found that neither STRO-1 nor CD133 isolated colony-forming endometrial stromal cells, even though STRO-1 was expressed on <10% of endometrial stromal cells. However, it showed that CD146 enriched for colony-forming cells, while cells with high levels of CD90 showed a trend to greater enrichment compared to low-expressing CD90 cells. CD146 was localised to perivascular cells of human endometrium. CD90 was strongly expressed in perivascular cells in the basal layer, but was also expressed on all stromal cells in the functional layer which sheds during menses. This study therefore identified CD146 as a marker of colony-forming human endometrial stromal cells. Further work using CD146 combined with another marker, PDGF-Rβ, has since led to the discovery of a method for prospectively isolating purified populations of human endometrial mesenchymal stem cells.

Schwab KE, Hutchinson P, Gargett CE (2008) Identification of surface markers for prospective isolation of human endometrial stromal colony-forming cells. *Hum Reprod*, 23:934-943.

Identification and hormonal regulation of a novel form of NKp30 in human endometrial epithelium

This paper reports the discovery of a novel form of the natural killer cell receptor, NKp30, in human endometrium. This receptor was previously thought to be exclusively expressed on natural killer cells, and to play a role in triggering cytotoxicity. We have shown that NKp30 is expressed by human endometrial luminal and glandular epithelial cells, with expression being increased during the late secretory phase of the menstrual cycle. The NKp30 protein is differentially glycosylated in comparison to the protein produced by NK cells, and expression is regulated by progesterone. Unexpectedly, clonally derived endometrial epithelial cells also expressed NKp30 at similar levels to fresh tissues, suggesting a fundamental role for this gene in endometrial biology. Although further work is required to understand the function of NKp30 in human endometrium, it is plausible that it may be involved in endometrial immune tolerance mechanisms that are a key component of successful pregnancy.

Ponnampalam AP, Gargett CE, Rogers PA (2008) Identification and hormonal regulation of a novel form of NKp30 in human endometrial epithelium. *Eur J Immunol* 38:216-226.

L to R: Dr Caroline Gargett, Prof Euan Wallis, Prof Peter Rogers, Dr Jane Girling

Grants received in 2008

NHMRC Project Grants

CE Gargett, GC Weston
Role of stem/progenitor cells in endometrial regeneration and in endometriosis (2009-2011)
$420,225

EM Wallace, SL Miller, G Jenkin, G Drummond, D Walker
Preventing prenatal brain injury in fetal growth restriction (2009-2011)
$491,125

Australian Research Council

DW Walker, H Dickinson
Who determines gestation length - mother or fetus? (2009-2012)
Discovery Grant and Australian Postdoctoral Fellowship, $400,000

Victorian Cancer Agency

ED Williams, DN Watkins, TG Johns, GE Hannigan, CE Gargett, ID Davis
Development of a high content screening platform for individualised cancer chemotherapy (2008)
$148,477

Philanthropic Grants

CE Gargett
Adult stem cells from the human uterus for pelvic floor prolapse surgery (2008)
L.E.W. Carty Charitable Fund, $35,040

H Teede
STOP diabetes: health related behaviour and risk perception in women with lifestyle related metabolic diseases at high risk of diabetes (2008-2010)
International Diabetes Federation, USD$360,825

S Tong
First trimester prediction of low birth weight; validation of a promising biomarker test that can be ordered at the first booking visit (2009)
Medical Research Foundation for Mothers and Babies, $30,000

Monash University Faculty of Medicine, Nursing & Health Sciences Strategic Grant Scheme

T Kaitu'u-Lino
The contribution of endometrial stem/progenitor cells to endometrial restoration after menses (2009)
Early Career Development Grant, $35,000

S Tong
Methotrexate packaged in a drug delivery vehicle that promotes tissue specific targeting; novel medical treatment for ectopic pregnancies (2009)
Early Career Development Grant, $35,000

Scholarships, awards and promotions

Pavitra Delpachitera
- 2008 Collaborative Bachelor of Medical Science Scholarship
- RANZCOG Research Foundation & Department of Obstetrics & Gynaecology, Monash University

Dr Caroline Gargett
- Appointed, Monash University Senior Research Fellow

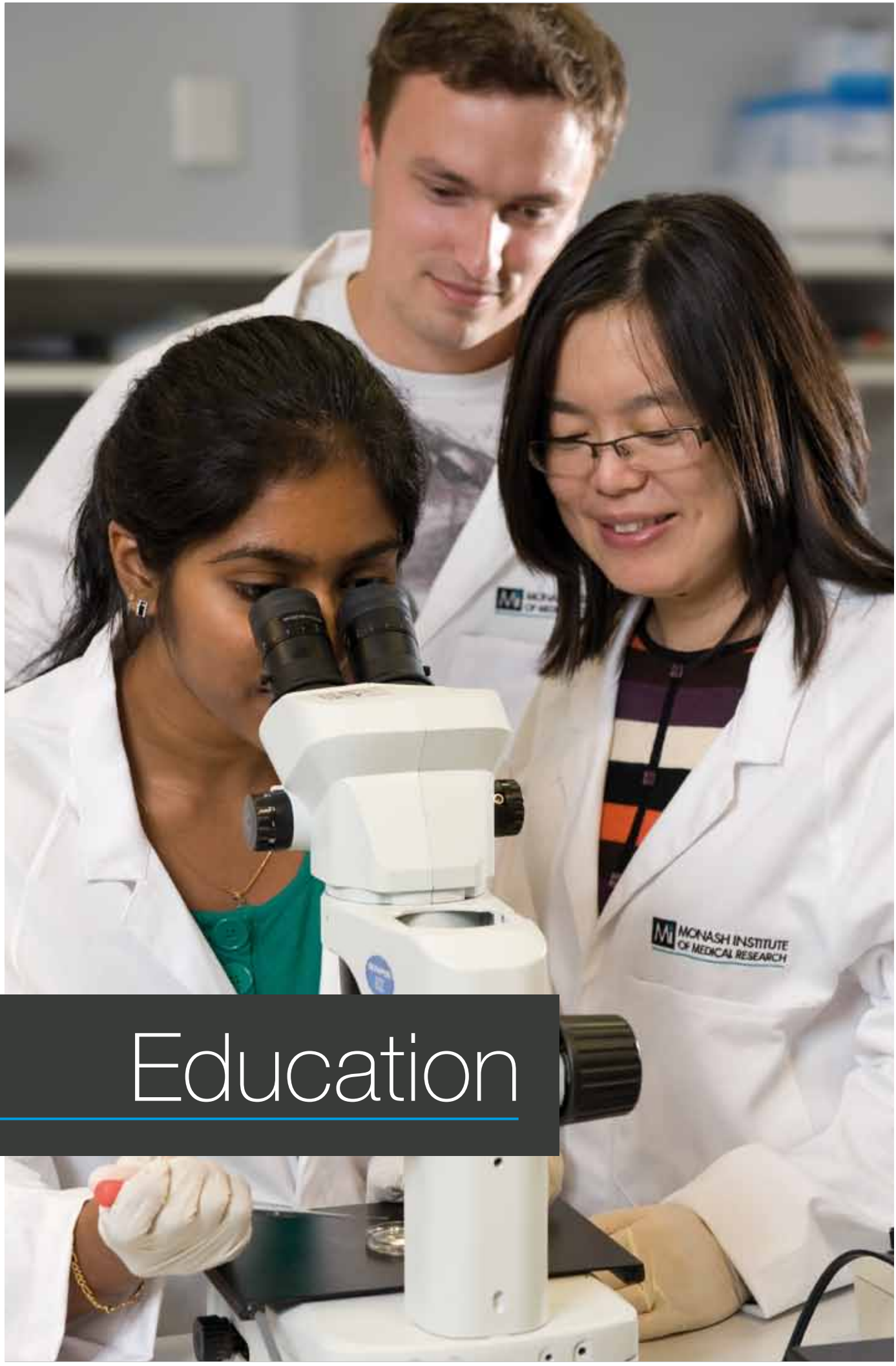
Dr Jane Girling and Dr Lisa Walter
- Best Scientific Presentation, 10th World Congress on Endometriosis, Melbourne

Dr Ryan Hodges
- Southern Health Emerging Researcher Fellowship
- Best Speaker Award, RANZCOG Provincial Fellows Conference 2008, Hervey Bay, Queensland

Dr Tu'uhevaha Kaitu'u-Lino
- Harold Mitchell Postdoctoral Travel Fellowship

Joanne Mockler
- Southern Health Emerging Researcher Fellowship

Dr Stephen Tong
- Royal Australian and New Zealand College of Obstetricians and Gynaecologists
- Arthur Wilson Scholarship (2008-2009)



Education

Education

Visiting Speakers 2008

MIMR's 2008 Seminar Series was proudly sponsored by DKSH.

Sue Sinni
Senior Program Advisor, Maternity Services/Metropolitan Health and Aged Care Services, Department of Human Services, Southern Health
Measuring patient safety in maternity services (4/3/08)

Dr Tetsuo Maruyama
Assistant Professor, Department of Obstetrics and Gynaecology, School of Medicine, Keio University, Tokyo, Japan
Regeneration potential and stem cells in the human female reproductive tract (11/3/08)

Dr Anne Voss
Laboratory Head, Development and Neurobiology Laboratory, Division of Molecular Medicine, Walter and Eliza Hall Institute of Medical Research
The role of the Ras signalling pathway molecule, C3G, in brain development (8/5/08)

Dr Keith McLean
Theme Leader, CSIRO Molecular and Health Technologies
Repair, replacement and regeneration: biomaterials research in CSIRO (22/5/08)

Drs Marcel and Claudia Nold
University of Colorado Health Sciences Center, Denver, Colorado, USA
IL-1F7: the answer to many questions? (26/6/08)

Dr David Mottershead
Haartman Institute, Department of Bacteriology and Immunology, University of Helsinki, Helsinki, Finland
GDF9, BMP15 and GDF3: stem cell derived TGF-β superfamily members (30/6/08)

Professor John Aitken
Director, ARC Centre of Excellence in Biotechnology and Development, University of Newcastle
Function and failure in the male germ line: a spermatozoon's perspective (3/7/08)

Professor Lex Doyle
Head, Clinical Research Development, The Royal Women's Hospital
The effect of changes in perinatal care over the past 50 years on outcomes for very tiny or preterm infants (17/7/08)

Jon Sherlock
Global Product Manager, Gene Expression, Applied Biosystems
Gene expression and regulation: new technologies enabling break-through research (28/7/08)

Dr Cristoph Konigs
JW Goethe University Hospital, Frankfurt/Main, Germany
Identification of antibody ligands and antigen specific B-cell targeting (5/8/08)

Professor David Hume
Director & CEO, The Roslin Institute, Scotland; Research Director, The Royal (Dick) School of Veterinary Studies, Scotland
Transcription control and macrophage biology (7/8/08)

Rebecca James
CEO, Research Australia
Capturing hearts and minds (14/8/08)

Professor Ian Fraser
Professor in Reproductive Medicine, Department of Obstetrics and Gynaecology, Queen Elizabeth II Research Institute for Mothers and Infants, Sydney University
Endometrial nerve fibres in women with endometriosis (18/8/08)

Dr Maria Dattena
Science Leader, animal physiology of reproduction, biotechnologies of reproduction, and stem cell studies, Agris-Sardegna, Italy
Biotechnologies of sheep reproduction in Sardinia (19/8/08)

Dr Ijad Madisch
Co-founder and creator of ResearchGATE
ResearchGATE – a platform for scientific networking (27/8/08)

Associate Professor Christine Clarke
NHMRC Principal Research Fellow, Westmead Millennium Institute, Westmead Hospital, Breast Cancer Research Group
Identification of progesterone targets in breast cancer (28/8/08)

Michael Spiegel
Deputy Director, Monash Antibody Technologies Facility (MATF)
Introduction to MATF (4/9/08)

Dr Kathy Traianedes
Principal Investigator, Australian Stem Cell Centre
Biological tissue regeneration (9/9/09)

Associate Professor Sarah A Robertson
Research Centre for Reproductive Health, University of Adelaide, South Australia
Seminal fluid signalling in the female reproductive tract and its role in immune adaptation for pregnancy (11/9/08)

Professor Dulal Panda
Professor and Head, School of Biosciences and Bioengineering, Indian Institute of Technology Bombay, Mumbai, India
Microtubules: dynamic targets for cancer chemotherapy (12/9/08)

Dr Paul A Trainor
Assistant Investigator, Stowers Institute for Medical Research, Kansas City, Missouri, USA
Making faces: the role of neural crest cells in craniofacial development and congenital birth defects (17/9/08)

Dr Ben Croker
Cancer and Haematology Division, The Walter and Eliza Hall Institute
Inflammation and autoimmunity caused by a SHP1 mutation depend on MyD88 and a microbial trigger (25/9/08)

Dr Carl N Sprung
Senior Research Officer, Division of Research, Peter MacCallum Cancer Centre
Investigating the molecular causes of clinical radiosensitivity (1/10/08)

Dr Marie-Liesse Asselin-Labat
Molecular Genetics of Cancer Laboratory, The Walter and Eliza Hall Institute
Gata-3, an essential regulator of mammary gland morphogenesis and luminal epithelial differentiation (7/10/08)

Professor Suzanne Cory
Director, The Walter and Eliza Hall Institute
The Bcl-2 family: an Achilles' heel for cancer (9/10/08)

Dr Kenneth Korach
Director, Environmental Disease and Medicine Program, Chief, Laboratory of Reproductive and Developmental Toxicology, National Institute of Environmental Health Sciences / National Institutes of Health, Research Triangle Park, North Carolina, USA
Consequences from the loss of estrogen receptor function (22/10/08)

Associate Professor David M Berman
Associate Professor of Pathology, Oncology, and Urology, The Johns Hopkins University Medical School, Baltimore, Maryland, USA
Deja vu all over again: how prostate and bladder cancers reuse developmental programs (6/11/08)

Professor Paul Gleeson
Head, Department of Biochemistry and Molecular Biology, Bio21 Molecular Science and Biotechnology Institute, The University of Melbourne
Manipulation of the membrane trafficking pathways in vivo using interference RNA (13/11/08)

Professor David Vaux
Department of Biochemistry, La Trobe University
Ten rules for the presentation and interpretation of data in publications (20/11/08)

Dr Raymond Kaempfer
Dr Philip M. Marcus Professor of Molecular Biology and Cancer Research, Faculty of Medicine, The Hebrew University Jerusalem, Israel; Visiting Academic: Centre for Cancer Research, MIMR
RNA sensors of stress signalling in the immune system (21/11/08)

Associate Professor Angelo DeMarzo
Sidney Kimmel Comprehensive Cancer Center at The Johns Hopkins University Medical School, Baltimore, Maryland, USA
Investigating the 'how' and 'why' in prostate cancer development (24/11/08)

Professor Hong Tang
Director, Centre for Infection and Immunity, Institute of Biophysics, Chinese Academy of Sciences, Beijing; Visiting Academic: Centre for Innate Immunity and Infectious Diseases, MIMR
How T-cells regulate innate inflammatory response to infection (26/11/08)

Dr Benjamin Kile
Queen Elizabeth II Fellow, Laboratory Head, Division of Molecular Medicine, Walter and Eliza Hall Institute of Medical Research
The molecular regulation of platelet production and function (27/11/08)

Professor Charles Cantor
Chief Scientific Officer, Sequenom Inc, San Diego, California, USA
Applications of nucleic acid mass spectrometry in cancer biology (1/12/08)

Professor Rob McLachlan
Group Leader, Male Reproductive Endocrinology and Metabolism, Prince Henry's Institute
Male hormonal contraception: a brief history (16/12/08)

Education Program in Reproduction and Development

The strategic priorities for the Education Program in Reproduction and Development (EPRD) in 2008 were to continue improvements in course structure, staffing and administration, to provide better training and equipment facilities for the larger class sizes, to improve research activities, and to complete preparations for the launch of an off-campus Master of Clinical Embryology (MCE) course in 2009. Strong support from staff at MIMR, Prince Henry's Institute, Monash Medical Centre and the Faculty of Medicine, Nursing and Health Sciences, ensured all EPRD students achieved the highest educational outcomes.

Improved laboratory and research facilities, combined with significant upgrades in training equipment during the year, continued to give our programs a strong competitive edge.

In 2008 the MCE course had its largest student enrollment. Students came from 13 countries and included 13 qualified medical practitioners. All students successfully completed the course, with 22 of the 25 graduates gaining employment in the IVF industry or research laboratories. Two students are planning to undertake further study.

Eleven students were enrolled in the Master and Graduate Diploma of Reproductive Sciences (MRS and GRS) courses. Four students completed the GRS in 2008. Three of these students will join the MCE course in 2009. Two current MRS students, Xiaoqian Wang and Jaqueline Sudiman, presented posters at the Endocrine Society of Australia and Society for Reproductive Biology Annual Scientific Meeting and at the Fertility Society of Australia Conference.

The increase in MCE student enrollments led to the recruitment of two academic staff, past EPRD graduates, Sarah Jansen and Penny Chen. The increase in student numbers also promoted greater collaboration with industry. There was a 30 percent increase in work experience placements locally, including all Australian states, and further expansion into Malaysian and Singaporean clinics.

EPRD introduced a vitrification short course in 2008. Vitrification is the most up-to-date method of cryopreserving gametes and embryos. The three vitrification workshops attracted Australian and international fertility specialists and provided an opportunity for highly trained clinical scientists to share ideas and develop expertise in this technique.

L to R: Dr Susan Cumming, Sarah Jansen, Liz Doidge, Penny Chen, Assoc Prof Peter Temple-Smith, Dr Sally Catt, Dr Mulyoto Pangestu

The three-year international collaboration with Gadjah Mada University in Indonesia continued to expand. In August, seven trainee obstetricians from Indonesia joined the MCE course for one month's training. Staff and students from universities in Jakarta, Yogyakarta, Bandung and Semarang also visited MIMR to participate, or discuss possible collaborations, in teaching and research.

During the year the Faculty approved the new MCE off-campus course, scheduled to begin in 2009. Initially this online course will only be offered to eligible Australian applicants, but enrollment of international students is planned in future years.

Despite the additional teaching load this year, EPRD has focused on developing a more significant research presence and establishing collaborations with other researchers. While many of these initiatives are still in the early stages of development, they will provide a base for future growth in our research quantum in 2009 and beyond.

MIMR Postgraduate Committee

The MIMR postgraduate committee provides a support and mentoring service for MIMR students and their supervisors. In 2008, there were 75 postgraduate students enrolled at MIMR. The committee, made up of representatives from each centre, meets monthly to review student progress and deal with any issues arising within the course of a particular student's studies. Both students and supervisors are able to approach the committee if problems arise, and in addition the committee requests that students attend regularly throughout their candidature to monitor progress. The committee treats all issues confidentially and aims to make the progress of each student towards the completion of their degree as seamless as possible.

The committee organises the University's formal requirements, such as confirmation of candidature after one year of enrolment and submission of annual progress reports. The committee also hosts an annual welcome barbecue in March, a Postgraduate Student Symposium for third and fourth year students, and a dinner for all students and supervisors in November.

Postgraduate Student Symposium

Sponsored by Invitrogen, the annual Student Symposium provides PhD students with the opportunity to present their research to their peers and Senior Scientists. The standard of the talks was impressive and covered a wide range of topics from stem cell research to sleep in infants and children.

The winners of the student prizes kindly donated by Invitrogen were:

Third Year

1st: Nicole Witcomb, Ritchie Centre for Baby Health Research
2nd: Burcu Saglan, Centre for Women's Health Research
3rd: Pollyanna Tat, Centre for Reproduction and Development

Fouth Year

1st: Brett Verstak, Centre for Innate Immunity and Infectious Diseases
2nd: Heidi Richardson, Ritchie Centre for Baby Health Research
3rd: Melissa Cooney and Cheryl Tay, Centre for Reproduction and Development

Fourth and Third-year Postgraduate Symposium winners, Brett Verstak and Nicole Witcomb.

MIMR's annual Student Open Day is designed to promote the diverse range of research opportunities available. The majority of students who attended the 2009 Open Day were enrolled in Biomedical Sciences or Science undergraduate courses at Monash University.

The tours of MIMR's seven research centres, conducted by student volunteers, were a highlight for the visiting students. Information kiosks in the de Kretser Concourse provided the opportunity for one-on-one interactions between prospective students and current trainees from each Centre.

One change instituted by the committee this year was to add Core Facilities (DNA sequencing, high content cellomics screening facility, imaging, and flow cytometry) to the Institute tours. This was a positive development and cited by student attendees as a worthwhile and interesting aspect of their visit. Thanks to Vivien Vasic, Camden Lo, James Ngui and Trevor Wilson for sharing their time and expertise for the benefit of prospective students.

The committee will be meeting early in 2009 to discuss the next Student Open Day. Innovative strategies for attracting students to MIMR in an increasingly competitive marketplace will be at the top of the committee's agenda.

2008 Graduates

Congratulations to the following students who completed their studies in 2008:

PhD

Prue Cowin, Centre for Urological Research:
Regulation of prostatic epithelial differentiation

Dr Garun Hamilton, Ritchie Centre for Baby Health Research:
Coronary vascular function in sleep and obstructive sleep apnoea

Rebecca Hobbs, Centre for Reproduction & Development:
Transforming growth factor-beta superfamily members and primordial follicle activation in the immature mouse ovary

Catherine Itman, Centre for Reproduction & Development:
Developmentally regulated SMAD signalling in the testis

Camden Lo, Centre for Reproduction & Development:
Nuclear localization of MAP2cN in the testis

Sridurga Prabhu, Centre for Reproduction & Development:
Regulation of KIT in spermatogenesis and hematopoiesis

Assoc Prof Kate Loveland, Centre for Reproduction and Development, with her 2008 graduates: L to R: Dr Catherine Itman, Dr Anette Szczepny, Assoc Prof Kate Loveland, Dr Camden Lo, Dr Sridurga Prabhu

Benjamin Rollo, Centre for Reproduction & Development:
The identification and function of reprogramming proteins in pluripotent cells

Anette Szczepny, Centre for Reproduction & Development:
Function and regulation of Hedgehog signalling in the adult mouse testis

Connie Wong, Centre for Innate Immunity & Infectious Diseases:
Oxidative stress and the cerebral microvasculature: a role for glutathione peroxidase-1

Stephanie Yiallourou, Ritchie Centre for Baby Health Research:
Development of cardiovascular control during sleep in infants: effects of sleeping position and implications for sudden infant death syndrome

Master of Philosophy

Oliver Heath, Centre for Reproduction & Development:
Development of defined conditions for human embryonic stem cell differentiation to definitive endoderm

Master of Biomedical Science

Alexandra Firsova, Centre for Reproduction & Development:
Isolation and differentiation of pluripotent cells from bovine embryos

Master of Biomedical Science (Part 1)

Nur Akmarina Mohd Said, Centre for Cancer Research:
Generation of a reporter system and screening for modulators of epithelial/mesenchymal transition

Shuya Lin, Centre for Reproduction & Development:
Effects of β-endorphin on endometrial stromal cells

Fangyuan Yang, Centre for Reproduction & Development:
Identification of adult stem cells during the mouse epididymal development

Bachelor of Biomedical Science (Honours)

Siti Anwar, Centre for Women's Health Research:
Identification of novel perivascular cell surface markers for prospective isolation of human endometrial mesenchymal stem-like cells

Marcin Ciula, Centre for Innate Immunity & Infectious Diseases:
Investigating the interaction between TRAF6 and STAT1

Andrea Clarke, Centre for Reproduction & Development:
Investigating the developmental potential of immature and failed to fertilize oocytes

Bachelor of Biomedical Science (Honours) *(cont.)*

Joanne Hepponstall, Ritchie Centre for Baby Health Research:
Autonomic cardiovascular control in preterm neonates with sleep disordered breathing

Janette Law, Centre for Women's Health Research:
The role of sex steroid hormones on angiogenesis in the mouse uterus

Kevin Luu, Centre for Innate Immunity & Infectious Diseases:
Investigating the interaction between TRAF6 and STAT3

Sewa Rijal, Centre for Reproduction & Development:
Characterisation of the mouse sperm acrosome and tail associated protein (SATAP)

Amanda Ross, Centre for Reproduction & Development and Centre for Urological Research:
Prenatal and postnatal development of the mouse epididymis

Georgina Ryland, Centre for Cancer Research:
The effects of integrin-linked kinase (ILK) inhibition on bladder cancer cells in vitro

Sebastian Stifter, Centre for Innate Immunity & Infectious Diseases:
Expression and purification of recombinant interferon epsilon

Padmini Sugamaran, Centre for Reproduction & Development:
Genetic infertility in mice and men

Bachelor of Behavioural Neuroscience (Honours)

Lalitha Krishnan, Ritchie Centre for Baby Health Research:
Development of cardiovascular control in full term infants: implications for sudden infant death syndrome

Leona Singam, Ritchie Centre for Baby Health Research:
Assessment of autonomic cardiovascular control in primary school children

Bachelor of Science (Honours)

Michelle Meilak, Centre for Innate Immunity & Infectious Diseases:
The impact of cytokine signalling on Toll-like receptor mediated immune responses

Agnieszka Pindel, Centre for Cancer Research:
The investigation of a role for PKR in atherosclerosis

Roxanne Toivanen, Centre for Urological Research:
Evaluation of CD133 as a marker of putative stem cells in benign and malignant prostate (Deakin University)

Bachelor of Science Advanced (Honours)

Nyssa Brown, Centre for Reproduction & Development:
An alternative method for sex selection in an agricultural livestock utilising the herpes simplex virus thymidime kinase suicide gene

Bachelor of Medical Science

Pavitra Delpachitra, Centre for Women's Health Research:
The pathogenesis of pre-eclampsia: activin-induced oxidative stress in endothelial cells

Michael Grant, Centre for Urological Research:
The effects of estrogen receptor beta agonists on prostate growth

Education Program in Reproduction and Development Graduates

Master of Clinical Embryology

Khalid Almady
Yang Chen
Huynh Nhu Giang
Anuradha Harishu
Abitha Jothinathan
Azif Kahn
Punyatrong Kiratikorn
Alice Lee
Kai Wern Lim
Krishna Mantravadi
Ishrat Meraj
Caroline Motteram
Radhakrishnan Muthukumar
Kheng Ling Ong
Anna Osborn
Zankruti Parmar
Prakash Pattnaik
Suran Rajapakse
Anamika Sakhuja
Ramya Sivanandam
Arivanban Thiruvalluvan
Adriana Villamizar
Azantee Abdul Wahab
Ziyuan Wu
Rajshekhar Yadav

Graduate Diploma in Reproductive Sciences

Kartini Asari
Hui Ling Carolyn Koon
Anjali Ninan
Sharona Ungar

Collaborative Ventures

Collaborative Ventures

CRC for Chronic Inflammatory Diseases

The Centre for Innate Immunity and Inflammatory Diseases (CIIID) is one of four groups that form the CRC for Chronic Inflammatory Diseases (CRC-CID), a national initiative comprising Monash University, the University of Melbourne, the University of Queensland and pharmaceutical company AstraZeneca.

In November 2005, the CRC-CID Board decided not to bid for another round of funding, so after seven years, the CRC-CID ceased operation on 30 June 2008. The first six months of the year, however, was an intense period in which CRC members concentrated on achieving their research outcomes.

CIIID Centre Director, Professor Paul Hertzog, in collaboration with Associate Professor Stuart Kellie from the University of Queensland, continued to focus their target validation research on the discovery of novel molecules and pathways that regulate macrophage interaction, in particular, signalling pathways governed by Toll-like receptors. One target has been validated as a therapeutic target for humans. Discussion is currently underway with commercial partners to further this exciting discovery.

Dr Trevor Wilson streamlined his research into target gene validation using in vivo systems, completing the production of genetically modified animal models for therapeutic target validation and reagents. Dr Nicole de Weerd and Leyla Zaker-Tabrizi continued to characterise interferon-receptor interactions in collaboration with Professor Jamie Ross-John's group at the Department of Biochemistry and Molecular Biology, Monash University.

Dr Ashley Mansell and Professor Paul Hertzog organised the *Innate Immune Sculpting of Adaptive Immunity* conference at Hamilton Island in April. This conference was held back-to-back with the Annual Scientific Meeting, and included national and international attendees.

CRC for Innovative Dairy Products

After supporting research and postgraduate students at Monash University for seven years, the Dairy CRC ceased operation on 30 June 2008. Throughout the 7 years, research support was in excess of $4 million, and educational support was provided for eight students who have either completed their PhD or are in the final stages of submission. In addition to completing their PhDs, these students also published eight manuscripts in peer-reviewed journals, and attended and presented their work at four international and three national scientific meetings in 2008.

Many other students benefited through the research support provided by the CRC to their laboratories. This has been a significant boost to the research and education programs for MIMR and the Centre for Reproduction and Development.

The CRC's school's Education Program was also closed. Most of the resources were transferred from the CRC GenEd website to the Learning Federation, which will continue to develop this as a resource in gene technology for primary and lower secondary schools. This secures a lasting legacy for the Dairy CRC program.

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. In 2008, this national program continued to raise awareness of men's health issues through community and professional education, and support of research.

A highlight for 2008 was a Men's Health Australia Longitudinal Study stakeholder forum which was held to gain input and support for a national men's health study. Hosted by Andrology Australia and the Governor of Victoria, Emeritus Professor David de Kretser AC, the forum was attended by more than 100 people representing government agencies, peak bodies, and chronic disease and population groups. The forum highlighted collaborative alliances and support for a national longitudinal study across the men's health sector.

Community education continued with Ambassador Merv Hughes speaking at a number of men's health events in regional areas. The Men's Health Education Kit was popular; almost 750 kits were distributed to assist communities to run successful men's health events. Andrology Australia's website hits continued to increase to more than 1.1 million, with 30,000 visitors and 17,500 downloads per month.

Andrology Australia became an endorsed provider of health professional education through the Royal Australian College of General Practitioners in 2008, allowing education programs to be developed and delivered direct to GPs. Online Active Learning Modules, GP summary guides and patient resources continued to be made available on the website to assist GPs in the management of their male patients.

For more information on Andrology Australia and men's health, visit www.andrologyaustralia.org

Supporting Our Research

Supporting Our Research

Monash Health Research Precinct Core Facilities

The Monash Health Research Precinct (MHRP) brings together scientists from MIMR, 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 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. These core facilities are managed by MIMR staff and scientists.

The evolution of the Core Facilities group continued throughout 2008. DNA sequencing, under the leadership of Vivien Vasic, gained several large, external clients as well as access to a second DNA sequencing instrument that has further improved throughput. Trevor Wilson continued to develop the High Content Screening system and additional equipment was purchased to help facilitate the storage of the human and mouse siRNA libraries. Lesley Wiadrowski now offers a time and cost-efficient mycoplasma screening assay. This assay can be performed in under an hour, is highly sensitive and picks up all known mycoplasma species.

Gandel Charitable Trust Sequencing Centre

The Gandel Charitable Trust Sequencing Centre has an excellent reputation for the provision of high quality sequence data to researchers and clinicians in the MHRP and numerous research institutes throughout Victoria.

Genetic analysis by DNA sequencing is an essential technology that is both a research tool for understanding gene structure as well as a diagnostic method, enabling the diagnosis of a number of inherited diseases. Demand for DNA sequencing has risen dramatically over the past three years. In 2008, the Collier Charitable Trust generously provided funding to the Centre, enabling the purchase of a second 16 capillary Genetic Analyzer. The instrument was funded jointly with the Clinical Genetic Laboratory (CGL) in Southern Health.

Sequencing Centre staff were able to take on a greater workload due to the improved capacity and technological benefits of the new sequencer. Usage by MIMR researchers, Precinct scientists and external clients such as the Ludwig Institute and CSL, increased by 25 percent.

The MHRP is committed to fostering the translation of basic research knowledge into clinical practice. Sharing technologies such as DNA sequencing will facilitate collaboration between the clinical and research areas of the Precinct, a key to achieving this aim.

Monash High Content Screening Facility

During 2008, the Monash High Content Screening Facility was established with funds obtained from the ARC LIEF Scheme, NHMRC, Monash University, the Faculty of Medicine Nursing and Health Sciences, and a number of University Departments and Research Groups.

The core pieces of equipment that make up the facility are a liquid handling robot to prepare large numbers of cell samples for analysis, and a ThermoFisher ArrayScan Instrument which enables automated imaging and analysis of the cells. The facility also has whole genome RNAi libraries, which enable researchers to individually inhibit every gene in the human or mouse repertoire and measure changes in specific cell functions.

The facility is currently being used by multiple groups from both MIMR and other Institutes to optimise assays.

Flow Cytometry Facility

The Flow Cytometry Facility provides diagnostic and research flow cytometry services for all scientists and staff at the MHRP.

Flow cytometry is a technique for counting, examining, and sorting microscopic particles suspended in a stream of fluid. Within the Precinct, this technology is currently employed by over 100 users performing research into autoimmune diseases, cancer, stem cells, human reproduction and development, microbiology and veterinary science.

An increasing reliance on flow cytometry and the addition of two new instruments in late 2007, has since seen an increase in usage by 20 percent.

Monash Gene Targeting Facility

The ability to target a specific gene in the mouse genome, to remove it, alter it or even replace it with the human equivalent, is a powerful tool used in basic and applied research with many applications to the study of human disease and determining gene function.

During 2008 the Monash Gene Targeting Facility (MGTF) continued to provide gene targeting services in mice to researchers throughout the Precinct.

Scientists and staff working in the MGTF provide tools for research into respiratory disease, the immune system, embryo development, the body's stress response, blood disease, muscle development, glucose transport in the body, the body's inflammation response, wound repair, cancer formation, hormone production, development of the central nervous system and the male reproductive tract.

Histology Laboratory

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

The relocation of the Histology Laboratory to larger premises and the purchase of a new tissue processor allowed laboratory staff to double its output.

MIMR Micro Imaging Facility

The MIMR Micro Imaging Facility provides sophisticated imaging platforms and analysis for all scientists and staff at the MHRP.

The facility provides consultation, reagents and imaging technologies encompassing timelapse and fluorescence imaging as well as sophisticated 3D reconstruction and Multiphoton imaging techniques. The expertise and technology enables researchers to study the intricate events of healthy and diseased biological systems, from organs and tissues down to molecules within cells.

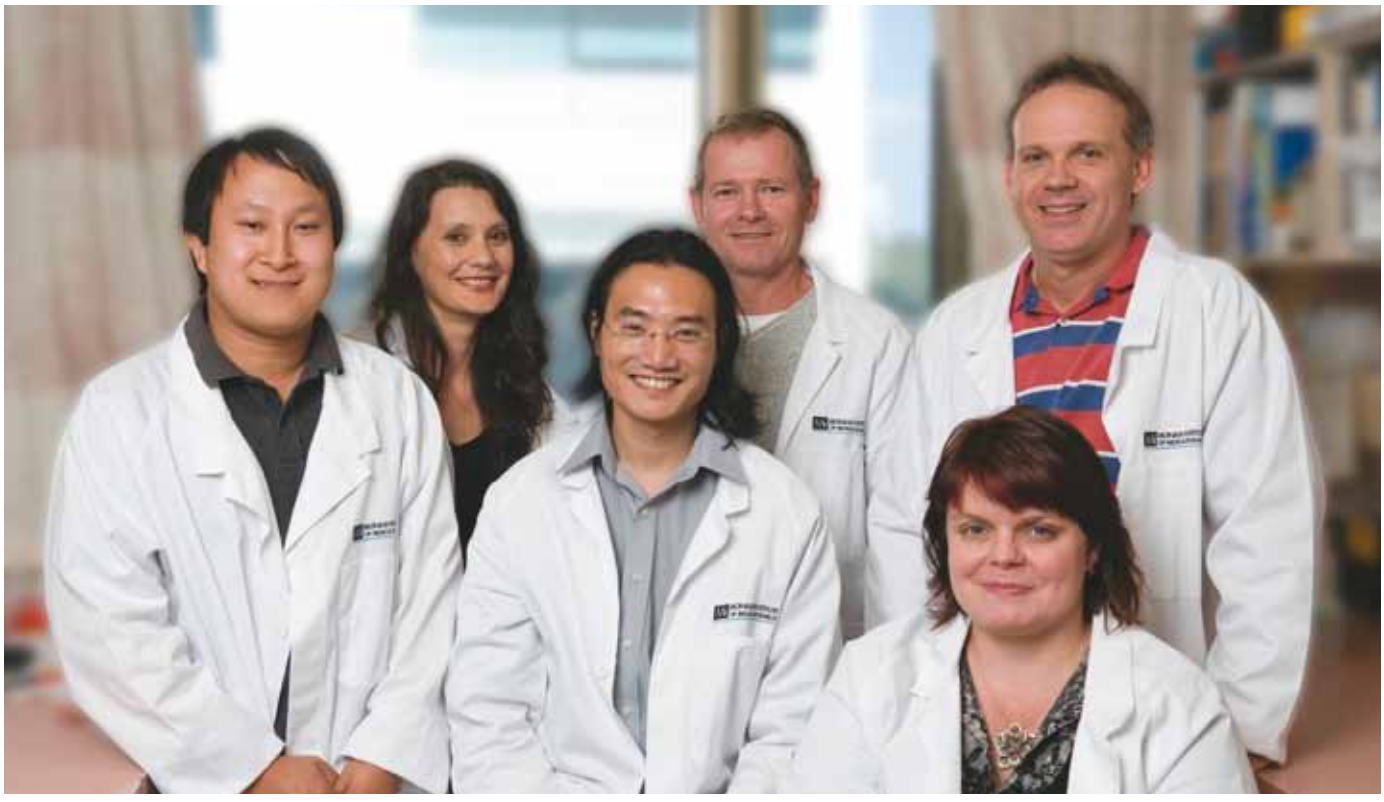
Monash Medical Centre Animal Facility

The first few months of 2008 were a challenge to the Monash Medical Centre Animal Facility (MMCAF) team as they struggled through normal daily work routines without major equipment that had been destroyed in the December 2007 flood. Persistence, teamwork and a lot of patience paid off and by mid-April the Facility was fully operational again.

Throughout 2008, MMCAF was also in the completion stages of the latest redevelopment which ensures a greater holding capacity for the Specific Pathogen Free (SPF) mice. The Facility expanded to include two Low Barrier areas, which hold a total of 27 racks. The High Barrier SPF area was re-established, allowing for expanding colonies of clean mice that will be used for embryo rederivation.

In 2008, the MMCAF team was joined by Project Officer, Shirine Chaudhry; Technical Officer, Michelle McMurtrie; SPF Supervisor, Jo Howden; Conventional Supervisor, Trevor Snow, and Materials Management Coordinator, Llain Evans.

Core Facilities, L to R: James Ngui, Dr Vivien Vasic, Dr Camden Lo, Dr Trevor Wilson, Dale Cary, Monika Generowicz



Monash Health Research Precinct Core Facilities *(cont.)*

Technology Services Group, Southern Regional

The Technology Services Group, Southern Regional provides IT service and support to MIMR, Prince Henry's and Monash University Faculty of Medicine, Nursing & Health Sciences staff and students. In 2008, the group delivered technology services that not only supported the business, but introduced innovation and development, to ensure the future needs of the business.

During the year, the team upgraded the entire network to gigabit Ethernet capacity. The handover of information technology infrastructure to Monash University was also completed. This will have a major impact on the team's ability to provide an enhanced level of service for many years to come.

MIMR Industry Engagement and Commercialisation

Over the last two years, MIMR has capitalised on innovation and discovery forged from previous years' research. From a "commercial" or tech transfer perspective, we have been in a renewable cycle phase focusing on translational and innovative research, which will lead to increased commercial activity in 2009/2010.

2008 saw a respectable level of industry engagement, with approximately $1.2 million of funds generated from commercial activities. In addition, a number of invention disclosures and patent applications from MIMR were filed, which should generate commercial interest as we progress through firming up commercial proof of concept data.

The indicators that allow us to measure industry engagement are not limited solely on return of revenues back to the Institute. There has been an increased activity in engaging with industry, as measured by the number of material transfer and confidentiality agreements that were processed in 2008. The fruits of that engagement should become apparent in the near future.

Dr Rocco Iannello

Administration

2008 was MIMR's most successful year, in terms of its total operating budget. The Institute received $28.9 million in total revenue, including $4 million direct research revenue, from Monash University, from our involvement with Monash IVF. These funds were used to establish the Carl Wood Endowed Chair in Obstetrics. All revenue sectors increased over the year and generated an overall operating surplus.

The administration function was formally reviewed by a panel of external and internal members to ensure Institute procedures and practices are of the highest possible standard, and that scientific staff are receiving efficient and relevant administrative support. The key recommendations of the Review will be implemented in early 2009.

L to R: Lisle Williams, Kaye Frith, Ganeema Tohki, Ann Scott, Brett Waldegrave, Lenette Griffin, Rod Wealands, Sandra Chittock, Russell Paulin, Rod Gillette, Rodney Edwards.

Development, Marketing and Communications

The Development, Marketing and Communications group is the link between our scientists and the community. Enhancing links with the community and improving understanding of MIMR scientist's research is a key objective.

MIMR reaches the community through media reporting of scientific results, participation in events such as the Australian Society for Medical Research (ASMR) Research Week activities and the annual Fresh Science competition. Institute publications and website also demonstrate the work of MIMR scientists and are available for community reference.

Throughout the year the Institute hosts regular tours for community groups, individuals, international visitors and student groups. Further, our scientists are frequently invited to visit community groups to discuss their latest research.

2007 saw the publication of *Biotechnology* (Oxford University Press) a resource for year 12 Biology students and teachers. In 2008, teacher workshops entitled 'Unravelling Biotechnology' were facilitated by Dr Susan Cumming, Education Manager, Centre for Reproduction and Development, who was co-author of the text. These were conducted in Victoria, New South Wales and Australian Capital Territory. Three of the 13 workshops were conducted at MIMR, with MIMR scientists as facilitators.

Community and Philanthropic Support

The Institute is fortunate to have many generous supporters and advocates including individuals, philanthropic trusts and foundations and corporate supporters and business leaders.

Institute scientists are highly successful in attracting major competitive research grants from organisations within Australia and from overseas. However, philanthropic support is needed to provide funding for a range of research projects and scientific equipment.

Throughout the year we have maintained regular contact with our supporters through our newsletter and direct mail appeals. We are grateful for our supporters' commitment and generosity. Our sincere thanks are extended to all our loyal donors who have given so generously to our direct marketing appeals.

During the year we received a number of gifts made in memory of family members or friends who have passed away or by those who have invited donations to MIMR in lieu of gifts to celebrate a birthday, anniversary or other special occasion. We are most appreciative of this support.

During the year, the Institute was fortunate to receive a bequest from the Estate of Mrs Patricia Penrose OAM, directed towards research into the causes and treatment for preeclampsia. Professor Euan Wallace, Clinical Director, Centre for Women's Health Research, leads the preeclampsia research program. He was pleased to invite members of Mrs Penrose's extended family to visit MIMR and discuss the significance this bequest will bring to his research.

In 2008, funds granted by a range of philanthropic trusts and foundations contributed to the funding of new research projects, the purchase of scientific equipment and student and travel scholarships. We were privileged to host a number of Trustees who visited the Institute to see first hand the outcomes of their generous support.

The Patrons Club and WISE (Women in Scientific Excellence) play an important role at the Institute. Club membership not only provides financial support but gathers a group of people who are interested in advancing medical research for the good of the community and can act as advocates for the Institute in the community. Members have the opportunity to develop a more informed understanding of current research and to meet the scientists whose work club membership supports.

Development, Marketing & Communications:
L to R: Andrea Carr, Susie Santilli, Julie Jacobs, Sue James

Ron Evans Golf Day

The second Ron Evans Golf day was held at Royal Melbourne Golf Club in November. The golf day is held to honour the memory of Mr Ron Evans AM and to raise funds for research into colon cancer.

Members of Ron's family, friends, colleagues and supporters of MIMR enjoyed a competitive game and awards dinner. The Ron Evans Perpetual Trophy was won by the Fox Sports team, comprising Danny Frawley, Tony Sinclair, Tony Shaw, and Matthew Campbell.

In 2008 the Institute announced the establishment of the Ron Evans Cancer Research Fellowship for colon cancer research. Funds raised at the annual golf day will be directed towards this Fellowship. The inaugural Fellowship was awarded to Dr Stephen Greenall from the Centre for Cancer Research.

We are grateful for the support and commitment of the Evans Family to this special golf day and for their support of our research into colon cancer.

We would like to thank the teams that participated and to acknowledge the fantastic support provided by the following people and companies who helped make the 2008 Ron Evans Golf Day a success.

Winners of the 2008 Ron Evans Perpetual Trophy - Fox Sports: Danny Frawley, Tony Sinclair, Tony Shaw, Matthew Campbell.

Below: 2008 Ron Evans Golf Day participants.

Golf Day Supporters

Mr Mark Allen
Australian Football League
Becco
Bennison Mackinnon
Chelsea Football Club UK
Mr Leigh Colbert
Cricket Australia
Elite Sports Properties
Essendon Football Club
Fosters Group Limited
Four Seasons Hotel, Sydney
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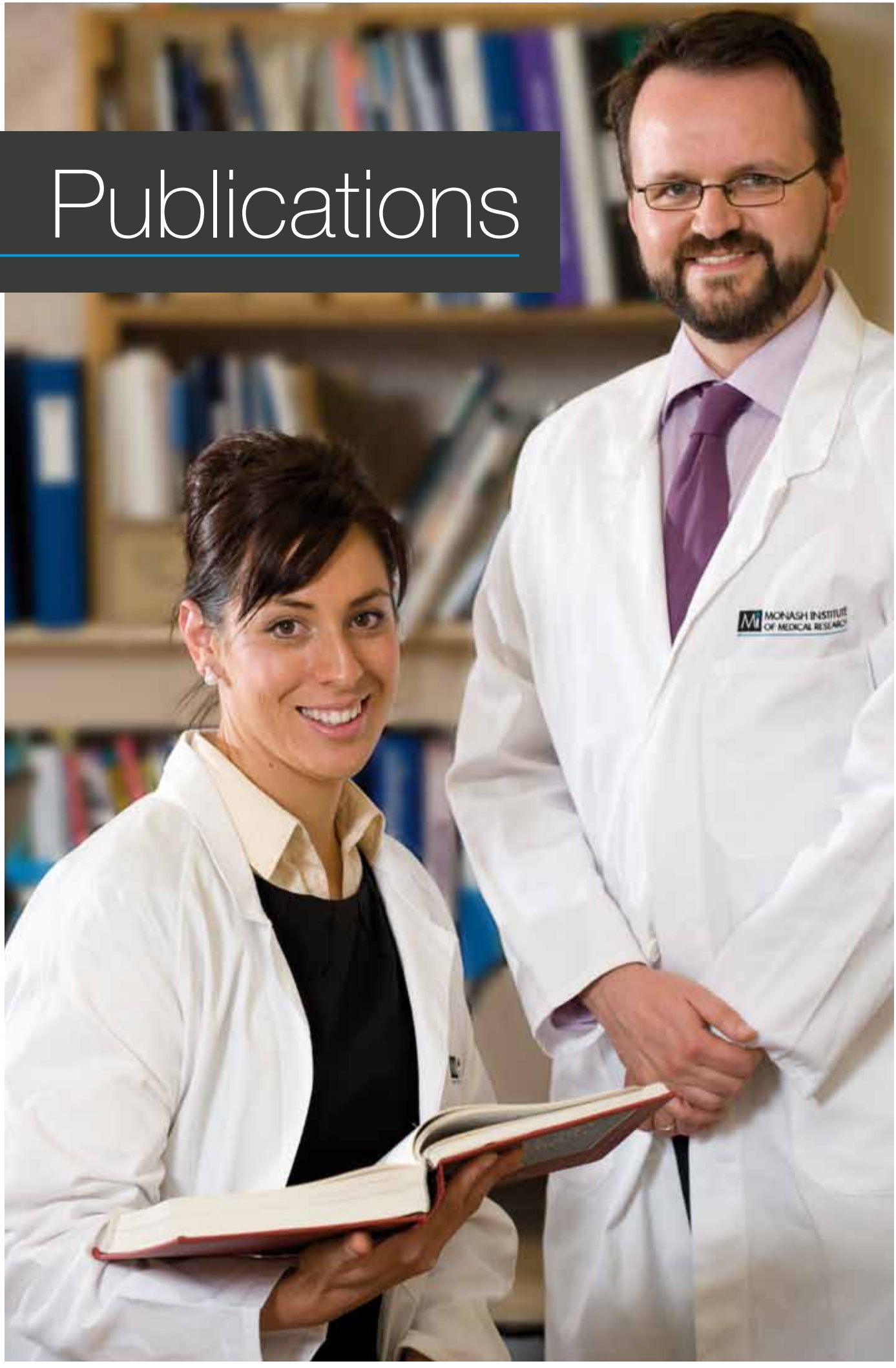

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Financial Report

Financial Report

Cash Flow Statement Year to Date 31 December 2008

	2008
Income	
General Revenue	5,741,989
Other Income	1,315,216
Commercial Services Income	712,884
Other Fees	
Student Course Fees	24,773
Investment Income	90,262
Non Research Funding	2,085,727
Scholarships & Prizes	42,377
Research Income	18,893,043
	28,906,271
Salaries Expenditure	
All Salary Expenses	14,589,967
	14,589,967
Non Salary Expenses	
Other Expenses	4,736,920
Financial & Admin Services	316,262
Travel & Related	902,762
Book & Library	58,733
Print & Stationery	377,219
Computer Related	429,000
Communications	390,486
Equipment Related	263,707
Lab & Operating	3,323,811
Student Related	320,977
Staff Related	83,228
Motor Vehicle	29,817
Building & Property	224,747
	11,457,669
Capital Expenditure	
Capital Expenditure	2,096,096
Operating Surplus/Deficit	762,539

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