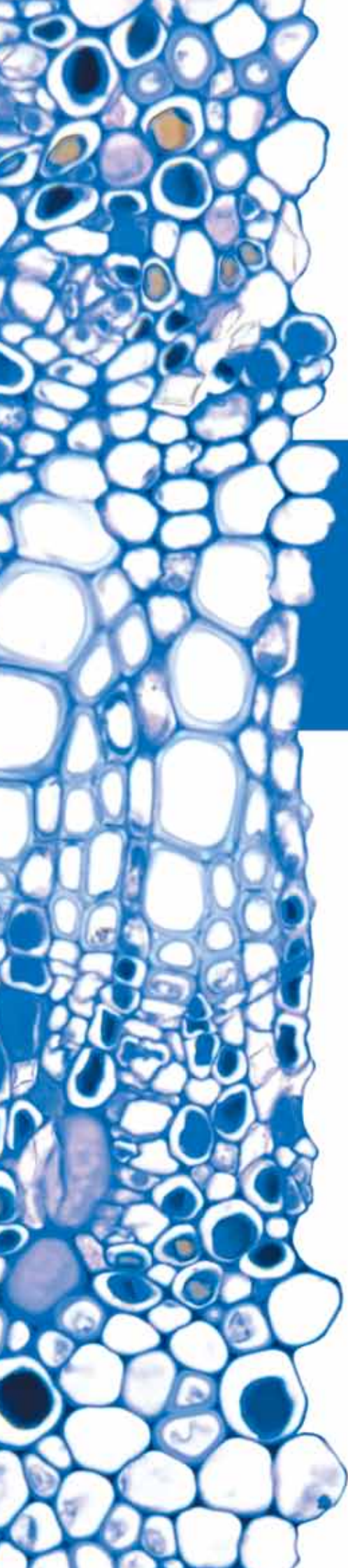

Annual Report 2009

MONASH INSTITUTE OF MEDICAL RESEARCH

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ABOUT **MIMR**

Emeritus Professor David de Kretser AO 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.

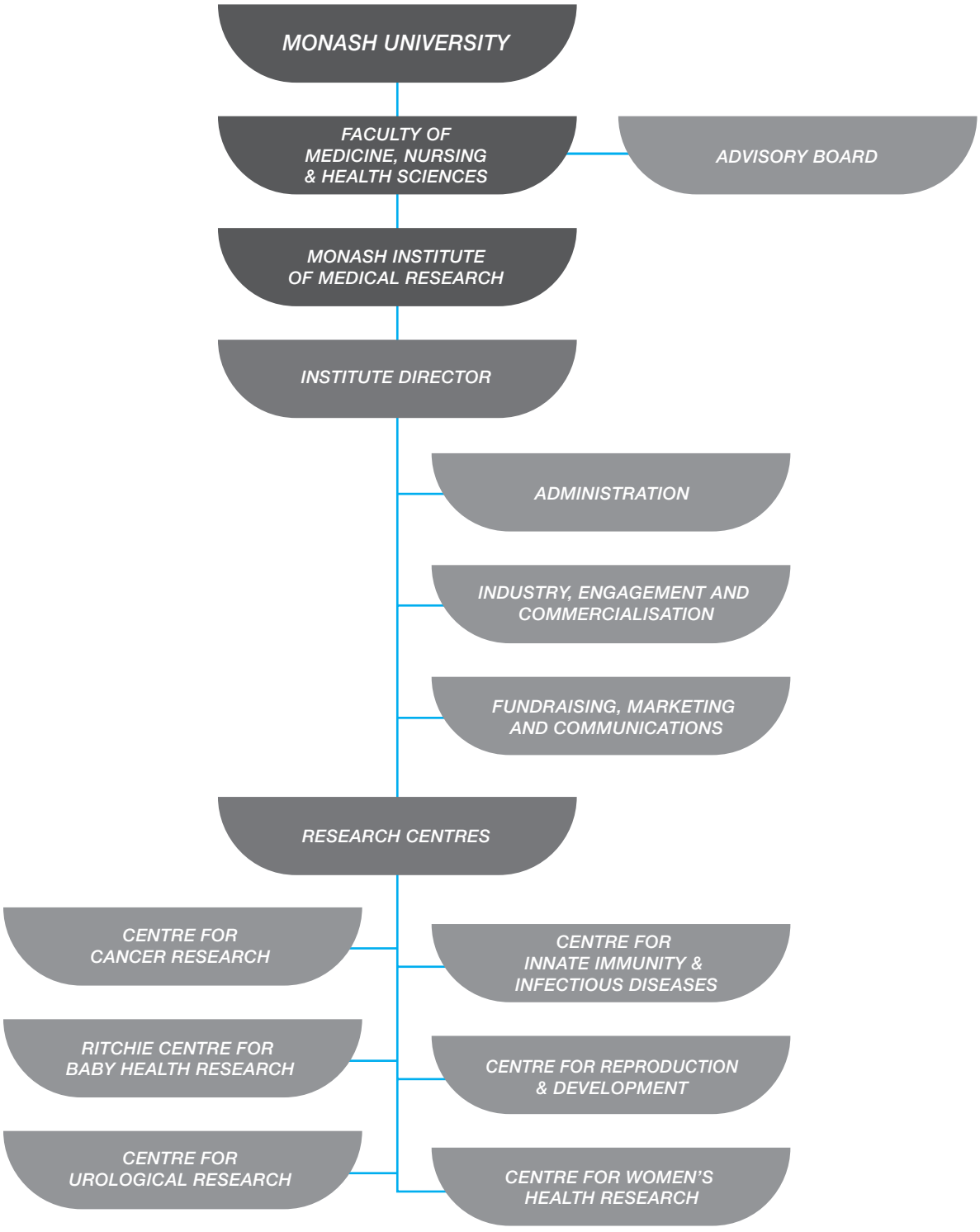
Over the years, the research conducted at the Monash Institute of Reproduction and Development (MIRD) benefitted many Australians, including infertile young people, parents of premature babies, and men with prostate cancer.

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 six research centres with a staff of over 300 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 and stem cells.

Following Professor de Kretser's retirement in 2005, Professor Bryan Williams, an internationally recognised cancer researcher, 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**

Partnerships, collaborations, translational research; it's all about connectivity. Connecting scientists, research findings, clinicians and patient outcomes is what we do best at MIMR. The 300 researchers, students and administrative staff who make up our Institute are dedicated to furthering our understanding of a wide range of diseases and medical problems.
Throughout 2009, we continued our mission to enhance human health and the quality of life by major research, innovation and discovery in biology, medicine and biotechnology research.

A major highlight was the Federal Government's decision to invest in a new translational research facility at the Monash Health Translation Precinct (MHTP). The $71 million commitment will support the building and equipping of a new facility to further integrate research along thematic lines and increase translational research and clinical activity. The MHTP partners, MIMR, Southern Health, Monash University and Prince Henry's Institute, will have an increased capacity for new joint research activities, and enhanced opportunities for the translation of basic laboratory research into clinical practice.

In 2009, the Institute continued to benefit from the Victorian Government's Operation and Infrastructure Support Program. This support, through the Department of Innovation, Infrastructure and Regional Development, ensures our Institute continues to operate smoothly and effectively.
At a more grassroots level, project funding from the National Health and Medical Research Council (NHMRC) is a major avenue of support for researchers undertaking biomedical research in Australia. MIMR researchers were successful in obtaining funding for 12 new projects, and were collaborators on another four projects. In addition, Associate Professor Rosemary Horne and Dr Richard Ferrero received NHMRC Senior Research Fellowships. These prestigious fellowships are awarded to outstanding biomedical researchers who have excellent track records in high-calibre research.
Forging internal connections, the MIMR Flagship Program entered its second year. The Flagship Program is an internal initiative that encourages our researchers to undertake a research project of high scientific and medical significance, with colleagues across the Institute. Led by Dr Stephen Tong, in collaboration with laboratory heads Professor Euan Wallace and Associate Professor Terry Johns, the project aims to test a novel medical treatment for ectopic pregnancies.
In the ever-changing world of medical research, we had a number of significant departures this year. Professor Gail Risbridger and her research team in the Centre for Urological Research transferred from MIMR to the Department of Anatomy at Monash University. Professor Risbridger will retain a strong affiliation with us and her team will continue to collaborate with MIMR researchers in the future.

The Centre for Reproduction and Development went through a major restructure in 2009. Centre Director, Professor Michael Holland joined the University of Queensland as Professor of Reproduction and Animal Biotechnology. Associate Professors Moira O'Bryan and Kate Loveland moved their groups to Monash University's Departments of Anatomy and Cell Biology and Biochemistry and Molecular Biology respectively. Although they are no longer based at MIMR, they will maintain strong links and collaborations with the Institute. We also bid farewell to Associate Professor David Phillips, who moved to LaTrobe University to become the Director of Research Services.

While these changes had an impact on the Centre for Reproduction and Development, it provided an opportunity to review the Centre's activities and to recruit a new Centre Director. We were very excited to announce the appointment of Professor Justin St John as the Centre's new Director. Professor St John is one of Britain's most respected reproductive biologists, whose research interests lie in understanding mitochondrial DNA and the role it can play in a range of debilitating diseases.

Also new to MIMR in 2009 was Dr Jason Lickliter, Director of Cancer Services at Peninsula Health. Dr Lickliter has taken up a joint appointment with MIMR to establish the Phase I Clinical Trials Program within the Centre for Cancer Research. We were also pleased to welcome Dr Richard Ferrero, who joined MIMR to head the Gastrointestinal Infection and Inflammation team within the Centre for Innate Immunity and Infectious Diseases.

As another busy, rewarding year draws to a close, it is satisfying to reflect on what we have achieved in 2009. I would like to thank and congratulate our researchers for their ongoing dedication and expertise. Thank you also to the administrative staff who so ably support our scientific and congratulate our researchers for their ongoing dedication and expertise. Thank you also to the administrative staff who so ably support our scientific endeavors It is our connections and collaborations within the Institute, throughout the MHTP, and further afield, that provide the resources, support and inspiration we need to continue to search for answers to biomedical questions that affect human health and quality of life.

Professor Bryan Williams
Institute Director

CHAIRMAN'S **MESSAGE**

It has been another busy, exciting and challenging year for researchers, students and staff at MIMR. We have continued to strengthen our translational research collaborations across the Institute, University and further afield.

A key strategic goal for the Faculty of Medicine, Nursing and Health Sciences for 2009 was the translation of biomedical research into improved health outcomes for patients. The Monash Health Translation Precinct is a partnership between MIMR, Monash University, Prince Henry's Institute and Southern Health. In early 2009, the Precinct partners were invited to submit a bid for Federal Government funding to build a dedicated translational research facility. This new facility will allow further integration of research along thematic lines and an increase in translational research and clinical trial activity. As a major announcement in the 2009/2010 Budget, the Government committed $71 million to fund the new, purpose-built translational research facility which will adjoin MIMR's existing buildings.

The State Government has since been approached for an additional $45 million to fully fund the project. While we are delighted that the Federal Government has invested in our facility, they will only release their funding once the State Government has given their final approval to provide the additional funding required. We will continue to work with both levels of Government to ensure that our long-held vision will become a reality.

A key action area in Victoria's Cancer Action Plan is the rapid translation of research into effective treatments and clinical care. An important part of this strategy is the development of cancer centres of excellence, including the Parkville Comprehensive Cancer Centre, the Olivia Newton-John Cancer Centre, and the Monash Comprehensive Cancer Consortium (MCCC). MIMR is well-represented within the MCCC, which aims to integrate research and clinical expertise in cancer, to promote translational research programs.

The development of a bio-imaging strategy for the University and Victoria was a key task this year. The establishment of an Imaging and Therapy Facility would be of great benefit to MIMR's cancer researchers, as they continue to investigate more effective ways of treating different cancers. Such a facility would also assist radiologists at the Monash Medical Centre who are also carrying out translational research.

Finally, I would like to thank all of the scientists, students, staff and Advisory Board Members of MIMR for their talent, dedication and support during 2009.

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

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

Advisory Board Member for Australia and New Zealand Oracle Corporation

National Deputy President, Australian Industry Group

Professor Nick Birrell

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

Venture Executive, Innovation Capital

Founder and former Chief Executive, Credit Suisse Asset Management Australia

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 & CRC Committee

Ms Barbara Crook

CEO, Taxpayers Australia

Mr Alastair Lucas

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

Member, Australian Government Takeovers Panel

Chairman, Burnet Institute

Professor Christina Mitchell

Head, School of Biomedical Sciences, Monash University

Member, Victorian State Government Science and Biotechnology Advisory Committee

Dr Hugh Niall

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

Former Chief Executive Officer, Biota

Chairman of the Diabetes Vaccine Development Centre

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

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

GOVERNANCE

ADVISORY BOARD

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 Steve Wesselingh

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

Director, Burnet Institute 2002-2007

Director, Infectious Diseases, Alfred Hospital, 1999-2002

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

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

Emeritus Professor Richard Larkins AO

Vice Chancellor, Monash University, 2003-2009

RESEARCH

CENTRE FOR **CANCER RESEARCH**

Prof Bryan Williams (Centre Director), Assoc Prof Terry Johns, Dr Elizabeth Williams, Assoc Prof Greg Hannigan, Prof Neil Watkins

Scientists in the Centre for Cancer Research undertake basic research into the molecular and cell signalling pathways that underlie the development, growth and metastasis of tumours, and the links with innate immunity and inflammatory processes. Scientists also work towards the development of novel cancer-targeting therapies and their translation to the clinic.

In 2009, the Centre for Cancer Research established a new Phase I Clinical Trials Program, in collaboration with Southern Health. Directed by Dr Jason Lickliter, Director of Cancer Services at Peninsula Health, the program aims to test the effectiveness of new therapies for the treatment of different cancers. This new program provides the Centre for Cancer Research with the potential to translate their laboratory findings into clinical applications.

Two new laboratories were established within the Centre for Cancer Research in 2009. Professor Wei Cheng, Director, Paediatric Surgery, Southern Health, will focus on the molecular mechanisms involved in gut development and regeneration. Dr Galina Polekhina was recruited to the Centre from St Vincent's Institute to create the Structural Biology Laboratory.

Associate Professor Terry Johns was awarded a Clinical Research Fellowship by the Victorian Cancer Agency for his research into glioblastoma, an aggressive cancer of the brain. His Fellowship will provide him with $400,000 over four years to examine the effects of targeting two tyrosine kinase receptors with monoclonal antibodies to block their activity.

Dr Dakang Xu received the 2009 MIMR High Profile Publication Award for his article in the high-impact journal Immunity. Dr Xu, Dr Anthony Sadler, Professor Bryan Williams and their collaborators showed for the first time that promyelocytic zinc finger protein (PLZF) plays a key role in the interferon response.

RESEARCH HIGHLIGHTS

A primary xenograft model of small-cell lung cancer reveals irreversible changes in gene expression imposed by culture in vitro

Emerging evidence suggests that the conventional cancer cell lines maintained in tissue culture are not ideal models for predicting the responses of cancers to novel therapies in patients. To address this issue in lung cancer, we used biopsy specimens from patients with newly diagnosed small cell lung cancer (SCLC) to generate a series of primary xenograft lines. These tumour models are maintained exclusively in immunodeficient mice, and faithfully maintain the growth pattern and phenotype of the primary tumours. Using a gene-expression array analysis of our model, researchers demonstrated that primary xenografts were more closely representative of SCLC tumours in patients than their derivative cell lines. Moreover, the study identified a characteristic gene signature whose expression is irreversibly lost in cell culture, all of which are critical determinates of tumour biology and therapeutic response. Researchers further extended the utility of these SCLC models to study tumour stem cell biology (Cancer, 2009; 69845-54), and to understand the genetic basis of acquired chemoresistance to conventional chemotherapy.

Daniel VC, Marchionni L, Hierman JS, Rhodes JT, Devereux WL, Rudin CM, Yung R, Parmigiani G, Dorsch M, Peacock CD, Watkins DN (2009) A primary xenograft model of small-cell lung cancer reveals irreversible changes in gene expression imposed by culture in vitro. *Cancer Res* 69:3364-3373.

JNK1 determines the oncogenic or tumor-suppressive activity of the integrin-linked kinase in human rhabdomyosarcoma

Rhabdomyosarcoma (RMS) is an aggressive skeletal muscle tumour that represents the most common solid tumour affecting children. Effective therapies for RMS have yet to emerge and molecular targets, for the development of RMS therapeutics, have not been identified to date. In this paper, researchers reported that the integrin-linked kinase, ILK, is hyperactivated in a particularly aggressive form of RMS. This activity of ILK promotes cell proliferation, and this work indicates for the first time that aberrant activation of ILK is a key factor in the development and spread of these aggressive tumours. Importantly, this study and others have shown that ILK activity can be targeted by selective small molecule inhibitors, providing an entirely new therapeutic strategy in RMS aimed at suppression of ILK's tumour-promoting activity. Moreover, ILK is hyperactivated in a number of cancers, suggesting a broader utility of targetting ILK to treat these tumours.

Durbin AD, Somers GR, Forrester M, Pienkowska M, Hannigan GE, Malkin D (2009) JNK1 determines the oncogenic or tumor-suppressive activity of the integrin-linked kinase in human rhabdomyosarcoma. *J Clin Invest* 119:1558-1570.

Antibodies specifically targeting a locally misfolded region of tumor associated EGFR

Epidermal Growth Factor Receptor (EGFR) is involved in stimulating the growth of many human tumours, but the success of therapeutic agents has been limited in part by interference from the EGFR on normal tissues. Previously, the researchers reported an antibody (mAb806) against a truncated form of EGFR found commonly in gliomas. Remarkably, it also recognises full-length EGFR on tumour cells but not on normal cells. However, the mechanism for this activity was unclear. Crystallographic structures for Fab:EGFR(287-302) complexes of mAb806 (and a second, related antibody, mAb175) show that this peptide epitope adopts conformations similar to those found in the wtEGFR. However, in both conformations observed for wtEGFR, tethered and untethered, antibody binding would be prohibited by significant steric clashes with the CR1 domain. Thus, these antibodies must recognize a cryptic epitope in EGFR. Structurally, it appeared that breaking the disulfide bond preceding the epitope might allow the CR1 domain to open up sufficiently for antibody binding. The EGFR(C271A/C283A) mutant not only binds mAb806, but binds with 1:1 stoichiometry, which is significantly greater than wtEGFR binding. Although mAb806 and mAb175 decrease tumour growth in xenografts displaying mutant, overexpressed, or autocrine-stimulated EGFR, neither antibody inhibits the in vitro growth of cells expressing wtEGFR. In contrast, mAb806 completely inhibits the ligand-associated stimulation of cells expressing EGFR(C271A/C283A). Clearly, the binding of mAb806 and mAb175 to the wtEGFR requires the epitope to be exposed either during receptor activation, mutation, or overexpression. This mechanism suggests the possibility of generating antibodies to target other wild-type receptors on tumour cells.

Garrett TP, Burgess AW, Gan HK, Luwor RB, Cartwright G, Walker F, Orchard SG, Clayton AH, Nice EC, Rothacker J, Catimel B, Cavenee WK, Old LJ, Stockert E, Ritter G, Adams TE, Hoyne PA, Wittrup D, Chao G, Cochran JR, Luo C, Lou M, Huyton T, Xu Y, Fairlie WD, Yao S, Scott AM, Johns TG (2009) Antibodies specifically targeting a locally misfolded region of tumor associated EGFR. *Proc Natl Acad Sci USA* 106:5082-5087.

The adhesion molecule L1 regulates transendothelial migration and trafficking of dendritic cells

The adhesion molecule L1, which is extensively characterised in the nervous system, is also expressed in dendritic cells (DCs), but its function there has remained elusive. To address this issue, we ablated L1 expression in DCs of conditional knockout mice. L1-deficient DCs were impaired in adhesion to and transmigration through monolayers of either lymphatic or blood vessel endothelial cells, implicating L1 in transendothelial migration of DCs. In agreement with these findings, L1 was expressed in cutaneous DCs that migrated to draining lymph nodes, and its ablation reduced DC trafficking in vivo. Within the skin, L1 was found in Langerhans cells but not in dermal DCs, and L1 deficiency impaired Langerhans cell migration. Under inflammatory conditions, L1 also became expressed in vascular endothelium and enhanced transmigration of DCs, likely through L1 homophilic interactions. Our results implicate L1 in the regulation of DC trafficking and shed light on novel mechanisms underlying transendothelial migration of DCs. These observations might offer novel therapeutic perspectives for the treatment of certain immunological disorders.

Maddaluno L, Verbrugge SE, Martinoli C, Matteoli G, Chiavelli A, Zeng Y, Williams ED, Rescigno M, Cavallaro U (2009) The adhesion molecule L1 regulates transendothelial migration and trafficking of dendritic cells. *J Exp Med* 206:623-635.

Promyelocytic leukemia zinc finger protein regulates interferon-mediated innate immunity

Interferons are naturally produced proteins that modulate the innate immune response and provide protection against viral infections and cancers. Interferons have been developed for clinical use over many years, and have been used in the treatment of diseases such as hepatitis, cancer and multiple sclerosis. Although much has been learned about their mechanism of action, the reason that some patients are more sensitive to treatment with interferons than others has proved difficult to identify.

The paper describes the discovery that promyelocytic leukemia zinc finger protein (PLZF) plays an important role in the immune response mediated by interferon. Interferon was shown to stimulate an association between PLZF and cofactors to switch on several key interferon-stimulated genes, including those involved in protection against viral infections. Mice lacking the gene that codes for PLZF were found to be more susceptible to infection with viruses. In addition, the activity of natural killer cells, which play an important role in the innate immune response, was impaired in mice lacking PLZF.

The results described in the study provide new insights into the mechanisms regulating the action of interferons, and demonstrate that PLZF is an important factor in the immune response. PLZF could therefore be used as a possible target for anti-viral and anti-tumour therapeutics.

Xu D, Holko M, Sadler AJ, Scott B, Higashiyama S, Berkofsky-Fessler W, McConnell MJ, Pandolfi PP, Licht JD, Williams BRG (2009) Promyelocytic leukemia zinc finger protein regulates interferon-mediated innate immunity. *Immunity* 30:802-816.

GRANTS AWARDED IN 2009

NHMRC Project Grants

M Febbraio, G Lancaster, BRG Williams, A Sadler
A novel lipid sensitive kinase and its role in obesity-induced inflammation and insulin resistance (2010-2012)
$540,075

G Hannigan, DN Watkins
The role of integrin linked kinase in hedgehog signaling and medulloblastoma (2010-2012)
$436,125

W Phillips, N Clemons, DN Watkins
Sonic hedgehog signalling in Barretts oesophagus (2010-2012)
$550,500

S Tong, TG Johns
Development of novel medical therapies to cure ectopic pregnancies (2010-2012)
$504,250

BRG Williams, D Xu
The role of PLZF in regulating the antiviral activity of interferons (2010-2013)
$622,800

NHMRC H1N1 Special Research Project

PJ Hertzog, K Visvanathan, A Mansell, J Sasaduesz, P Reading, BRG Williams
Development of a signature for early responses to influenza strains that determine/correlate with severity of infection, vaccine response and changes in virulence (2009-2010)
$313,063

NHMRC Equipment Grants

R Andrews, C Gargett, I Harper, M Hickey, S Jackson, D Jans, B Jenkins, K Loveland, U Manuelpillai, R Medcalf, DN Watkins, E Williams
Establishment of MMI advanced microscopy platforms for live cell and intravital imaging (2009)
$220,000

Z Andrews, J Armitage, R Brown, I Clarke, M Cowley, K Denton, R Evans, M Kett, M Lackmann, C Mitchell, B Oldfield, M Rosa, E Simpson, J Smith, S Spencer, B Strauss, T Tiganis, A Tilbrook, D Walker, M Watt, BRG Williams,
DEXA body composition and bone density analysis suite (2009)
$220,000

Australian Research Council Linkage, Infrastructure, Equipment and Facilities Grant

M Wilce, T Beddoe, S Bottomley, P Hertzog, J Rossjohn, J Whisstock, BRG Williams, N Cowieson, M Hearn
Biomolecular small angle x-ray scattering facility (2009)
$500,000

Cancer Council Victoria Venture Grant

P Rogers, D Blakey, R Lewis, I Svarb, BRG Williams
The biological effects of synchrotron microbeam radiation therapy on normal and tumour tissues (2009-2010)
$206,500

Cancer Council Victoria Project Grant

S Selemidis, ED Williams, G Drummond
Novel pharmacological targets for suppression of tumour angiogenesis (2009-2012)
$300,000

Victorian Cancer Agency Clinical Fellowship

TG Johns
Dual targeting of the EGFRvIII and c-Met tyrosine kinase receptors in glioblastoma (2009-2012)
$400,000

MIMR Flagship Project Grant

S Tong, T Johns, E Wallace
Novel medical treatments for ectopic pregnancies in humans (2010)
Monash Institute of Medical Research, $100,000

SCHOLARSHIPS, AWARDS AND PROMOTIONS

Sanja Coso
- Highly Commended, Southern Health Research Week, Poster Award, Cancer Research

Sheetal Deshpande
- Cancer Council Vacation Studentship

Anton Kolosov
- Faculty of Medicine, Nursing and Health Sciences Scholarship

Renaud Quantin
- Australian Postgraduate Award Scholarship

Alex Wilding
- Faculty of Medicine, Nursing and Health Sciences Postgraduate Research Scholarship

Dr Simon Wilkins
- Highly Commended, Southern Health Research Week, Poster Award, Paediatric Research

Dr Dakang Xu
- 2009 MIMR High Profile Paper Publication Award

CENTRE FOR **INNATE IMMUNITY & INFECTIOUS DISEASES**

Assoc Prof Brendan Jenkins, Dr Richard Ferrero, Prof Paul Hertzog (Centre Director), Dr Ashley Mansell

The past year has been one of further development for the Centre for Innate Immunity and Infectious Diseases. A highlight was the recruitment of Dr Richard Ferrero and his group from Monash University Department of Microbiology. Dr Ferrero brings a new research dimension to the Centre, with his expertise in the pathogenesis of infectious disease from the perspective of the pathogen. Furthermore, his work integrates aspects of the pathogen with an understanding of the host cell response. His special area of research is in Helicobacter pylori; bacterial infections found in the stomach that gives rise to ulcers, and, in the case of longer infections, to chronic gastritis and its predisposition to gastric cancer. These areas complement the pre-existing fields of research in the Centre and the physical movement of his group will improve collaborative research outputs.

The Centre made excellent progress in one of its missions to build on years of expertise in functional genomics research to perform more genome-scale analysis of immune responses to disease. This was achieved by publication of INTERFEROME; a database and associated analytical tools. Its popularity and utility is testified by the 50,000 hits in its first year. Researchers capitalised on this breakthrough by receiving a grant for genomics analysis of patient responses to swine flu. This enabled consolidation of the Centre's bioinformatics capability.

Work in the Molecular Immunity Group made solid progress on determining the structure of interferon-receptor interactions, characterisation of a new cytokine with functions in the reproductive tract and the role of interferons in autoimmune disease such as systemic lupus erythematosus and other inflammatory diseases.

Research undertaken by the Toll-Like Receptor Group, led by Dr Ashley Mansell, was recognised in the prestigious *Journal of Biological Chemistry*. Their work described the molecular mechanism of action of MAL; a key innate immune signal transduction molecule.

The Centre continued to nurture high-achieving postgraduate students. Two students undertaking the Bachelor of Biomedical Science (Honours), Sam Forster and Lori Turner, both finished top of their respective departments' Honours lists. Our PhD students were very successful in winning travel awards to present their work and promote the Centre and Institute at international meetings.

Our profile was highlighted by ongoing research with our international collaborators. The well-established collaboration between Associate Professor Brendan Jenkins' group

and Simon Jones' group in Cardiff, Wales continued to be productive, as evidenced by the 2009 publication in the *Journal of Immunology* based on research into inflammatory arthritis. This collaboration will be further enhanced in 2010 with a post-doctoral researcher from Professor Jones' group joining Associate Professor Jenkin's group for one year to continue the arthritis research.

The MONMAN program to develop novel mouse models for the study of inflammation and cancer made solid progress with our colleagues in Manitoba, Canada. In addition, researchers convened a special workshop in Canada with international experts in immunology discussing the cellular interactions in inflammatory responses.

RESEARCH HIGHLIGHTS

INTERFEROME: the database of interferon regulated genes

This paper describes a database established by scientists in the Centre for Innate Immunity and Infectious Diseases to aid in the analyses of complex datasets. The advances in technology associated with sequencing the human genome and its approximately 28,000 genes have also generated the ability to determine when these genes are activated or inactivated – so called expression profiling. Scientists can now measure how the expression of all 28,000 genes is changing in a given situation, such as in specific diseases and responses to therapy. The data generated in such experiments is enormous and the ability to store, validate, analyse and interpret presents new challenges.

This challenge has yielded the relatively new field of bioinformatics. INTERFEROME, the database created by MIMR researchers, contains many experiments detailing expression profiling of responses to interferons and proteins produced by the body in response to disease stimuli such as infection, inflammation or cancer. The data contained is unique and scientists have devised many new and different ways to aid interpret complex amounts of data to identify useful trends.

This database can be used to analyse datasets from infectious disease, inflammatory disease and cancers for novel innate immune pathway activation.

In its first year, INTERFEROME has had 50,000 hits, which is indicative of its utility. In addition, the analytical tools developed in this database have also enabled MIMR reserarchers to win competitive grants for studies such as the NHMRC–funded swine flu project. This funding will allow scientists to undertake gene profiling of patient responses, which will enable scientists to tease out the complex responses, such as susceptibility or resistance to infection or vaccination, of individual patients.

Samarajiwa SA, Forster S, Auchettl K, Hertzog PJ (2009) INTERFEROME: the database of interferon regulated genes. *Nucleic Acids Res* 37:D852-857.

MyD88 adapter-like (Mal)/TIRAP interaction with TRAF6 is critical for TLR2- and TLR4-mediated NF-kappaB proinflammatory responses

The early, innate immune response of a cell to a disease stimulus is the critical, first step in orchestrating the production of regulatory cytokines; chemokines that attract inflammatory cells to the site of disease. This initial response will determine whether the next stages in the response are disease resolution; chronic (inflammatory) disease; severe, acute inflammation such as septic shock or SARS; autoimmunity or even death. This paper describes the molecular detail of how the innate response is triggered by innate receptors called toll-like receptors and adaptor molecules that bind to them inside the cell and transmit signals that initiate the cell response. This study details how the adaptor molecule, MAL, functions inside the cell. Knowledge of this kind will be useful in advancing understanding of inflammatory disease and responses to infections, the possible development of targeted anti-inflammatory drugs, and biomarkers of disease.

Verstak B, Nagpal K, Bottomley SP, Golenbock DT, Hertzog PJ, Mansell A (2009) MyD88 adapter-like (Mal)/TIRAP interaction with TRAF6 is critical for TLR2- and TLR4-mediated NF-kappaB proinflammatory responses. *J Biol Chem* 284:24192-24203.

GRANTS AWARDED IN 2009

NHMRC Research Fellowship

R Ferrero
Senior Research Fellowship Level A (SRFA) (2010-2014)

NHMRC Project Grants

P Crack, P Hertzog
The role of interferon signalling in the regulation of stroke (2010-2012)
$598,500

P Hertzog, H Reid
Structural characterisation function analyses of type I interferon-receptor interactions (2010-2012)
$499,500

NHMRC H1N1 Special Research Project

P Hertzog, K Visvanathan, A Mansell, J Sasaduesz, P Reading, BRG Williams
Development of a signature for early responses to influenza strains that determine/correlate with severity of infection, vaccine response and changes in virulence (2009-1010)
$313,063

NHMRC Equipment Grants

R Andrews, C Gargett, I Harper, M Hickey, S Jackson, D Jans, B Jenkins, K Loveland, U Manuelpillai, R Medcalf, DN Watkins, E Williams
Establishment of MMI advanced microscopy platforms for live cell and intravital imaging (2009)
$220,000

T Beddoe, W Charman, A Christopoulos, G Drummond, P Hertzog, C Mackay, J Rossjohn, P Scammells, P Sexton, J Whisstock
High throughput analysis and screening facility (2009)
$325,000

Australian Research Council Linkage, Infrastructure, Equipment and Facilities Grant

M Wilce, T Beddoe, S Bottomley, P Hertzog, J Rossjohn, J Whisstock, BRG Williams, N Cowieson, M Hearn
Biomolecular small angle x-ray scattering facility (2009)
$500,000

SCHOLARSHIPS, AWARDS AND PROMOTIONS

Sam Forster
- University Medal for Academic Excellence, awarded for receiving the highest mark in a Bachelor of Biomedical Science (Honours) degree for 2009

Ka Yee Fung
- International Society for Interferon and Cytokine Research Travel Grant
- Monash University Travel Grant

Claire Greenhill
- International Society for Interferon and Cytokine Research Travel Grant
- Rotary Club of Kew Travel Grant
- Monash University Travel Grant

Angel Ho
- Cancer Council Vacation Studentship with Assoc Prof Brendan Jenkins

Assoc Prof Brendan Jenkins
- Appointed as Associate Professor

Tali Lang
- Hepatitis B Foundation Student Travel Award

Louise McLeod
- Winner, Southern Health Research Week Poster Award, Inflammatory and Infectious Diseases Research

Dr Niamh Mangan
- Seymour and Vivian Milstein Young Investigator Award for notable contributions to research

Saleela Ruwanpura
- Ian Potter Foundation Travel Grant
- Monash University Travel Grant

Dr Belinda Thomas
- Third prize, MIMR Scientific Retreat Poster Presentation

Lori Turner
- Ed Westaway Prize for the top-ranked Microbiology Honours student, Faculty of Medicine, Nursing and Health Sciences

CENTRE FOR **REPRODUCTION & DEVELOPMENT**

Dr Paul Verma, Assoc Prof Mark Hedger (Deputy Centre Director), Dr Ursula Manuelpillai, Prof Justin St. John (Centre Director)

The Centre for Reproduction and Development conducts research into how human disease develops and is transmitted. Scientists in the Centre use innovative reproductive, developmental and stem cell biology approaches to further their research. In 2009, scientists in the Centre further consolidated their expertise in mitochondrial genetics, amnion and pluripotent stem cell derivation, oocyte and embryo reconstruction and hormonal function and immune response in the male reproductive system.

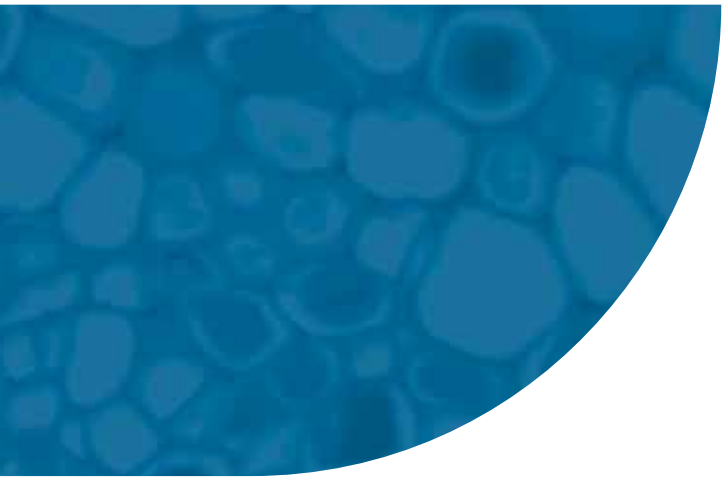
Research carried out by two of the Centre's senior scientists was recognised with significant grants from the NHMRC. Dr Ursula Manuelpillai received $596,500 to further her research into how human amnion cells (cells found in the placenta following birth) may be used to treat fibrosis of the liver. Dr Manuelpillai also received $12,100 from the Arthur A Thomas Trust to investigate how the body may respond to amnion cell transplantation.

Associate Professor Mark Hedger continues the Centre's renowned work into the role the hormone follistatin may play in reproductive biology, with a $591,500 NHMRC grant.

Throughout 2009, Dr Paul Verma continued to work on producing induced pluripotent stem (iPS) cells; cells from a part of the body such as skin that are reprogrammed to act as embryonic stem cells. Dr Verma received funding from the Australian Stem Cell Centre to continue this research. In addition, he received commercial grants from US company, Viagen, and Stem Cell Technologies Singapore to fund his research into the generation of iPS equine (horse) stem cells.

This year, the Centre underwent a period of significant change. Centre Director, Professor Michael Holland, was appointed Professor of Reproduction and Animal Biotechnology at the University of Queensland. Associate Professor Moira O'Bryan moved her group to Monash University Department of Anatomy and Cell Biology, and Associate Professor Kate Loveland moved her team to the Department of Biochemistry and Molecular Biology. And, after 15 years at MIMR, Associate Professor David Phillips moved to LaTrobe University to become the Director of Research Services.

Using these changes as an opportunity to review key research areas for the Centre for Reproduction and Development, the Institute appointed Professor Justin St. John as the new Centre Director in November. Professor St. John brought his research program based on mitochondrial DNA transmission and replication from the University of Warwick in the UK. This added a new dimension to the Centre by expanding the developmental biology and stem cell work into mitochondrial genetics, with an emphasis on understanding the transmission of genetic disease. Further review and expansion of the Centre will continue in 2010.



RESEARCH HIGHLIGHTS

Human umbilical cord mesenchymal stem cells reduce fibrosis of bleomycin-induced lung injury

Acute respiratory distress syndrome (ARDS) is characterised by loss of lung tissue resulting from inflammation and fibrosis. ARDS affects approximately 75 per 100,000 people in developed countries with a 40-60% mortality rate. As currently available interventions are not wholly effective or safe in the long term, a collaborative project between the Lung Institute of Western Australia and the Monash Institute of Medical Research was established to test a stem-cell based therapy to reduce inflammation and fibrosis and restitute the lung epithelium. Bleomycin-injured mice were used and Wharton's jelly mesenchymal stem cells (WJ-MSCs), obtained from umbilical cord of term placenta. WJ-MSCs administered systemically were found up to two weeks in inflamed and fibrotic regions but did not show evidence of differentiation into lung epithelium. Mice-administered cells had reduced pro-inflammatory cytokines IFNγ, TNFα and MIF and significantly reduced collagen levels. Mechanistically, this may have been due to reduced TGFβ, a pro-fibrotic cytokine, reduced TGFβ induced Smad2 signalling and to increased collagen degrading MMP-2 together with reduced levels of the MMP inhibitors the TIMPs. These effects were seen over the four-week test period even in the absence of WJ-MSCs in the mouse lungs. Notably, WJ-MSCs were not retained in healthy mouse lungs nor were these effects found in mice administered lung fibroblasts following bleomycin administration.

These findings suggest that WJ-MSCs may be useful in the development of future cellular therapies for ARDS.

Moodley Y, Atienza D, Manuelpillai U, Samuel CS, Tchongue J, Ilancheran S, Boyd R, Trounson A (2009) Human umbilical cord mesenchymal stem cells reduce fibrosis of bleomycin-induced lung injury. *Am J Pathol* 175:303-313.

Effects of chronic celecoxib on testicular function in normal and lipopolysaccharide-treated rats

The enzyme COX-2 catalyses production of prostaglandin E2 (PGE2), which regulates processes such as inflammation and vasodilation. To investigate the function of COX-2 and PGE2 in the testis, rats were fed chow containing celecoxib, a common anti-inflammatory drug and inhibitor of COX-2. The drug regime successfully reduced testicular PGE2 levels by 60%. COX-2 was essential for controlling fluid levels in the rat testis, with an increase in testicular interstitial fluid levels occurring after COX-2 inhibition. Celecoxib also protected against the damaging effects of bacterial LPS on testicular weight, interstitial fluid levels and serum testosterone, but had no effect on cytokine levels in the testis. These results indicate significant roles for COX-2 and PGE2 in testicular vascular control and steroidogenesis. This may have implications for men with marginal fertility taking celecoxib for extended periods, but it also highlights the potential of this drug to ameliorate testicular damage caused by systemic or local inflammation.

Winnall WR, Muir JA, Liew S, Hirst JJ, Meachem SJ, Hedger MP. (2009) Effects of chronic celecoxib on testicular function in normal and lipopolysaccharide-treated rats. *Int J Androl.* 32(5):542-555.

GRANTS AWARDED IN 2009

NHMRC Project Grants

J Girling, M Hedger, P Rogers, D de Kretser
Novel roles for follistatin in reproductive biology (2010-2012)
$591,500

U Manuelpillai, W Sievert
Role of human amnion epithelial cells in resolving hepatic fibrosis (2010-2012)
$596,500

NMHRC Dora Lush Biomedical Postgraduate Scholarship

H Wu
Activin A - a link between inflammation and diabetes and hypercholesterolemia (2009-2011)
$68,031

NHMRC Equipment Grant

R Andrews, C Gargett, I Harper, M Hickey, S Jackson, D Jans, B Jenkins, K Loveland, U Manuelpillai, R Medcalf, DN Watkins, E Williams
Establishment of MMI advanced microscopy platforms for live cell and intravital imaging (2009)
$220,000

Australian Stem Cell Centre Grant

P Verma
Generate mouse and human induced pluripotent cell lines without genetic modifications (2009-2011)
IPSC Research Program, $354,000

Contract Grants

P Verma
Sex selection: an application of embryonic stem cell technology project (2010-2013)

Dairy Australia Ltd (Australian Commonwealth Government), $420,000

P Verma
Generation of induced pluripotent stem cell lines from defined cell populations (2009)
Mesoblast, $135,500

P Verma
Development of putative induced pluripotent stem cells from the horse (2009)
Stem Cell Technologies, Singapore, $15,000

Philanthropic grants

U Manuelpillai
Host immune responses to human amnion epithelial stem cell transplantation (2009)
Equity Trustees – Arthur A Thomas Trust, $12,100

SCHOLARSHIPS, AWARDS AND PROMOTIONS

Dr Claire Borg
- World Health Organization International Travel Award, American Society of Andrology

Dr Yi Chen
- TAG Medical Young Achiever Award, Australasian Society of Thoracic and Cardiac Surgeons annual scientific meeting

Dr Vinali Dias
- Trainee Merit Award - American Society for Andrology Trainee Awards

Assoc Prof Mark Hedger
- Elected President of the Society for Reproductive Biology, 2009-2012

Corey Heffernan
- Australian Stem Cell Centre International Travel Award
- Third prize, MIMR 2009 Postgraduate Student Symposium

Dr Catherine Itman
- New Investigator Award - American Society for Andrology Trainee Awards

Dr Duangporn Jamsai
- 2009 Lalor Foundation Travel Award, American Society of Andrology

Dr Ursula Manuelpillai
- Faculty of Medicine, Nursing and Health Sciences Travel Award

Gita Pratama
- 2009 Australian Society for Stem Cell Research, Poster Presentation Award

Pollyanna Tat
- Monash Travel Award
- Canadian Stem Cell Network AGM Poster Presentation Award
- Second prize, MIMR Postgraduate Student Symposium
- Second prize, MIMR Scientific Retreat Poster Presentation

RITCHIE CENTRE FOR BABY HEALTH RESEARCH

Assoc Prof Rosemary Horne (Scientific Director), Dr Phillip Berger (Acting Centre Director), Dr Andrew Ramsden (Clinical Director), Dr Gillian Nixon

The Ritchie Centre for Baby Health Research is devoted to research in developmental science, focussing on the medical problems of the newborn infant. Through their close partnership with Southern Health, researchers have access to patients under clinical care. The Centre is strongly committed to translating its scientific knowledge into improved medical treatments via commercial partnerships and patenting of its discoveries.

In 2009, the Ritchie Centre researchers were again recognised by the NHMRC. Scientific Director, Associate Professor Rosemary Horne, was reappointed as an NHMRC Senior Research Fellow for a further five years. In addition, Associate Professor Horne was invited as Visiting Professor to the University of Picardie Jules Verne, Amiens, France for six weeks.

Acting Centre Director, Dr Philip Berger, was awarded an NHMRC project grant to develop a new method for quantifying the degree of instability in patterns of breathing common in preterm infants and patients with heart failure. Dr Berger will apply this method to developing effective treatments for these patients.

Dr Alex Veldman was awarded an NHMRC project grant for a collaborative study into preventing lung disease in preterm infants, using human amnion cells.

During the course of the year, seven of the Centre's students; Drs Priscila Cassaglia, Bradley Edwards, Susan Feng, Heidi Richardson, Nicole Whitcomb, Flora Wong and Joel Yang were awarded their PhD degrees. Some have taken up their first postdoctoral appointments overseas and some have continued to expand their research through postdoctoral positions at MIMR and Southern Health.

The Centre continued its tradition of promoting strong clinical-scientific partnerships. Dr Reshma Silas was appointed Ritchie Clinical Fellow to work with Dr Flora Wong on control of the cerebral circulation in preterm infants. Dr Gillian Nixon was appointed Senior Research Fellow/Senior Respiratory Physician in partnership with the Southern Health Department of Respiratory Medicine and the Melbourne Children's Sleep Unit. Dr Nixon is an investigator on a number of projects related to paediatric sleep and breathing.

In August, more than 70 guests attended the annual Kaarene Fitzgerald Lecture, which provides the public, health professionals and researchers with up-to-date research findings on Sudden Infant Death Syndrome and related issues. The keynote speaker was Professor Caroline Blackwell, Conjoint Professor of Immunology and Microbiology at the University of Newcastle. Other speakers included Dr Heidi Richardson, Dr Stephanie Yiallourou and Nicole Whitcomb from the Ritchie Centre. Dr Yiallourou was appointed the Kaarene Fitzgerald Fellow, 2009-2011.

The Ritchie Centre expanded its research base with the recruitment of Dr Claudia Nold, from the University of Colorado, Denver, USA. She joined the Ritchie Centre as the Blair C Ritchie Fellow to continue her work on cytokine biology. The Centre was also bolstered by the appointment of Dr Marcel Nold as a Fellow within Monash Newborn; a position that enables him to continue his research into the role of inflammation in the newborn.

RESEARCH HIGHLIGHTS

A model analysis of arterial oxygen desaturation during apnea in preterm infants

Rapid arterial O_2 desaturation during apnea in the preterm infant has obvious clinical implications but to date no adequate explanation for why it exists. Understanding the factors influencing the rate of arterial O_2 desaturation during apnea is complicated by the non-linear O_2 dissociation curve, falling pulmonary O_2 uptake, and by the fact that O_2 desaturation is biphasic, exhibiting a rapid phase (stage one) followed by a slower phase when severe desaturation develops (stage two). Using a mathematical model incorporating pulmonary uptake dynamics, we found that elevated metabolic O_2 consumption accelerates the rate of desaturation throughout the entire desaturation process. By contrast, the remaining factors have a restricted temporal influence: a low pre-apneic alveolar oxygen level causes an early onset of desaturation, but thereafter has little impact; reduced lung volume, hemoglobin content and cardiac output, accelerate desaturation during stage one, and finally, total blood O_2 capacity (blood volume and hemoglobin content) alone determines the rate of desaturation during stage two. Preterm infants with elevated metabolic rate, respiratory depression, low lung volume, impaired cardiac reserve, anemia, or hypovolemia, are at risk for rapid and profound apneic hypoxemia. Our insights provide a basic physiological framework that may guide clinical interpretation and design of interventions for preventing sudden apneic hypoxemia.

Sands SA, Edwards BA, Kelly VJ, Davidson MR, Wilkinson MH, Berger PJ (2009) A model analysis of arterial oxygen desaturation during apnea in preterm infants. *PLoS Comput Biol* 5:e1000588.

Minimising the risks of sudden infant death syndrome: to swaddle or not to swaddle?

Swaddling, or firm wrapping, is a traditional infant care practice that has been used in some form by various cultures since ancient times. Recently, swaddling has been promoted as a means to settle infants for sleep on their backs. Sleeping infants on their backs is recommended to protect infants from Sudden Infant Death Syndrome (SIDS). Despite this recommendation, there have been limited studies investigating the effects of swaddling on infant sleep and more particularly arousal from sleep. A failure of arousal from sleep in response to a prolonged pause in breathing is a likely mechanism for SIDS.

As part of her PhD, Heidi Richardson carried out a study that examined the effects of swaddling in infants who were routinely swaddled at home and those who were not.

The study found that swaddling had no effect on the arousability of infants who routinely slept swaddled at home. However, a significant decrease in both total arousability and frequency of full or cortical arousal was observed in the infants who were not accustomed to being swaddled. These findings suggest that arousal suppression may not simply be a consequence of swaddling per se, but rather, of being unfamiliar with sleeping swaddled.

The findings have important implications for child care practices, as infants are often placed in unfamiliar sleeping environments when mothers return to work, and so it is important for secondary carers to fully consider this. By identifying potential new risks associated with naïve swaddling, this study has highlighted the importance of thorough scientific investigation prior to widespread recommendations for changes in infant care practices.

Richardson HL, Walker AM, Horne RS (2009) Minimizing the risks of sudden infant death syndrome: to swaddle or not to swaddle? *J Pediatr* 155:475-481.

GRANTS AWARDED IN 2009

NHMRC Research Fellowship

R Horne
Senior Research Fellowship Level A (SRFA) (2010-2014)

NHMRC Project Grants

P Berger, G Hamilton, M Naughton
Duty ratio: a simple method for quantifying loop gain during breathing instability (2010-2012)
$331,841

E Wallace, G Jenkin, T Moss, S Miller, A Veldman
Preventing preterm lung disease - a cell therapy approach (2010-2012)
$444,189

NHMRC Equipment Grants

G Hamilton, R Horne, M Lenne, M Naughton, T Sletten, J Stout, S Wilson Rajaratnam
The Cambridge Neuropsychological Test Automated Battery (CANTAB) (2009)
$100,000

G Hamilton, D O'Driscoll, B Strauss, S Wilson Rajaratnam
The SenseWear PRO3 Armband and ancillary equipment (2009)
$17,000

Baxter Bioscience Grant

A Veldman, P Berger
Chronic lung disease in the preterm neonate: investigating the protein C pathway as potential therapeutic target (2009)
Baxter Bioscience Grants (non-clinical research), $180,000

Thoracic Society of Australia and New Zealand

B Edwards
The mechanisms underlying the aging predisposition to obstructive sleep apnea (2009-2010)
Allen & Hanburys Respiratory Research, $140,000

Philanthropic Grants

L Walter
Harold Mitchell Foundation Postdoctoral Travel Fellowship (2009), $5000

B Edwards
Harold Mitchell Foundation Postgraduate Travel Fellowship (2009), $5000

S Yiallourou
Kaarene Fitzgerald Fellowship (2009-2011)
SIDS and Kids Vic, $60,000

MIMR Flagship Project Grant

S Tong, T Johns, E Wallace
Testing the efficacy of a novel combination therapy to treat ectopic pregnancies (2010)
Monash Institute of Medical Research, $100,000

SCHOLARSHIPS, AWARDS AND PROMOTIONS

Dr Denise O'Driscoll

- Heart Foundation Travel Grant, 11th International Symposium on Sleep and Breathing, Pittsburgh, Pennsylvania, USA

CENTRE FOR
UROLOGICAL RESEARCH

Prof Gail Risbridger (Centre Director), Dr Renea Taylor

Researchers working in the Centre for Urological Research conduct basic and translational research into the three clinical conditions that affect the prostate gland: prostate cancer, benign prostate hyperplasia and prostatitis. The Centre's research is divided into two broad areas: stem cells (in prostate and breast cancer) and the role reproductive hormones play in the onset of prostate disease.

Close affiliations with universities, hospitals and other institutes complement the Centre's research. In addition, researchers participate in a number of collaborations and consortia, including the Prostate Cancer BioResource, the Victorian Prostate Cancer Research Collaboration and Andrology Australia.

Two grants from the Prostate Cancer Foundation of Australia (PCFA) in 2009 will enable researchers to further their investigations into the role estrogens play in prostate disease. This funding from PCFA is integral in allowing the Centre's researchers to assess the potential utility of a novel drug for men suffering from prostate cancer.

Dr Kara Britt was successful in obtaining two grants from the Victorian Cancer Agency in 2009. She was awarded an Early Career Seed Grant for her research project *Influence of estrogen on mammary epithelial stem cell numbers and how this relates to breast cancer risk*. The Link and Learn Grant Dr Britt received enabled her to travel to the Breakthrough Cancer Research Centre, Institute of Cancer, London, UK.

Roxanne Toivanen received the inaugural PhD scholarship from the Rotary Club of Canterbury. Roxanne, a first-year PhD student, is growing models of prostate cancer using tissues from patients with the disease, to develop new therapeutic options.

We were saddened to hear of the passing of George Limb in March. Researchers at MIMR, and in particular, the Centre for Urological Research, will remember the legacy he has left. In 2007, George and his wife Janet provided funding for the Limb Family Foundation Scholarship, for two PhD students undertaking prostate cancer research. Shirin Hussain and Sarah Wilkinson were the inaugural recipients. While George will be sadly missed by all who knew him, his memory will live on through the scholarships he has provided.

RESEARCH HIGHLIGHTS

Lineage enforcement by inductive mesenchyme on adult epithelial stem cells across developmental germ layers

During development, cell differentiation is accompanied by the progressive loss of pluripotent gene expression and developmental potential. De-differentiation in specialised cells, however, can be induced by reprogramming strategies. This indicates that transdifferentiation potential is retained in adult cells. The stromal niche provides differentiating cues to

epithelial stem cells, but current evidence is restricted to tissue types within the same developmental germ layer lineage.

Anticipating the use of adult stem cells for tissue regeneration, this study examined if stroma can enforce lineage commitment across germ layer boundaries and promote transdifferentiation of adult epithelial stem cells. Results showed tissue-specific mesenchyme instruct epithelial cells from a different germ layer origin to express dual phenotypes. Prostatic stroma induced mammary epithelia (or enriched mammary stem cells) to generate glandular epithelia expressing both prostatic and mammary markers. Gene array analysis implicated hedgehog and Wnt pathways in mediating stromal-epithelial interactions. Other recombinants of prostatic mesenchyme and skin epithelia, or preputial gland mesenchyme and bladder or esophageal epithelia, showed foci expressing new markers adjacent to the original epithelial differentiation, confirming altered lineage specification induced by stroma and evidence of cross-germ layer transdifferentiation.

Thus, stromal cell niche is critical in maintaining (or re-directing) differentiation in adult epithelia. In order to use adult epithelial stem cells in regenerative medicine, researchers must additionally regulate their intrinsic properties to prevent (or enable) transdifferentiation in specified stem cell niches.

Taylor RA, Wang H, Wilkinson SE, Richards MG, Britt KL, Vaillant F, Lindeman GJ, Visvader JE, Cunha GR, St John J, Risbridger GP (2009) Lineage enforcement by inductive mesenchyme on adult epithelial stem cells across developmental germ layers. *Stem Cells* 27:3032-3042.

Increased endogenous estrogen synthesis leads to the sequential induction of prostatic inflammation (prostatitis) and prostatic pre-malignancy

There is a growing body of evidence supporting a role for inflammation in the development of carcinoma in a number of tissues, including the prostate. However, the causes of prostatitis represent a significant gap in knowledge with 90-95% of cases having an unknown aetiology. It is imperative, therefore, to identify the causes of prostatitis to improve our understanding of this disease and its role in prostate cancer (PCa).

Estrogens may be a cause of prostatitis and in this study we examine the effect of aromatase over-expression (and thus elevated estrogen levels) in a murine model (AROM+ mouse). The study showed that although the prostates of these mice develop normally, there are progressive changes during life that culminate in the development of pre-malignant lesions. Growth of the gland is reduced at puberty and there is a significant elevation in mast cell numbers. Upon further aging, chronic inflammation emerges and pre-malignant PIN-like lesions developed by 52 weeks of age.

Overall, this study links estrogens to inflammation and pre-malignancy of the prostate, further implicating estrogen in the induction and/or progression of PCa. The data also shows that the AROM+ mouse is a novel, non-bacterial model for the study of prostate inflammation.

Ellem SJ, Wang H, Poutanen M, Risbridger GP (2009) Increased endogenous estrogen synthesis leads to the sequential induction of prostatic inflammation (prostatitis) and prostatic pre-malignancy. *Am J Pathol* 175:1187-1199.

GRANTS AWARDED IN 2009

NHMRC Project Grants

G Risbridger, R Taylor, D Berman
Defining stromal-cancer cell interactions for xenografting human prostate cancer (2010-2012)
$539,500

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

NHMRC Enabling Grant (renewed funding for a further 5 years)

J Clements, G Risbridger
Australian Prostate Cancer Collaboration (APCC) Bio-Resource (2010-2014)
$2,100,000

Australian Research Council Discovery Grant

G Risbridger, R Taylor
Keeping stem cells on track (2009-2011)
$307,000

Cancer Council Victoria (CCV)

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

Victorian Cancer Agency

G Risbridger, R Taylor, E Williams
To establish a Human Prostate Cancer Stem Cell Program (2009-2010)
$419,538

Victorian Cancer Agency Victorian Prostate Cancer Research Consortium Grant

G Risbridger
Establishment of a human prostate stem cell program (2009–2010)
$419, 538

Victorian Cancer Agency Early Career Seed Grant

K Britt
Influence of estrogen on mammary epithelial stem cell numbers and how this relates to breast cancer risk (2009)
$45,908

Victorian Cancer Agency Link and Learn Grant

K Britt
Travel to Breakthrough Breast Cancer Research Centre, Institute of Cancer Research, London, UK (2009)
$4,308

Prostate Cancer Foundation of Australia / Cancer Australia (co-funded award)

I Davis, G Risbridger, C Nelson, R Taylor
Mechanisms of abiraterone resistance in prostate cancer (2010-2012)
$589,500

Prostate Cancer Foundation of Australia Project Grants

G Risbridger, R Taylor
Novel estrogen therapy for advanced prostate cancer (2010-2012)
$250,000

G Risbridger, R Taylor
Targeting prostate cancer stem cells with beta selective estrogen receptor modulators (2009)
$93,743 (interim funding)

Prostate Cancer Foundation of Australia Young Investigator Award

S Ellem
Estrogens in prostatitis and prostate cancer (2009)
$93,495 (interim funding)

Health Research Council of New Zealand

E Gold, G Risbridger, H Nicholson
Role of activin C in prostate disease (2009-2012)
$953,000

Philanthropic Grant

K Britt
Does a woman's exposure to estrogen, which modulates breast cancer risk, affect the mammary stem activity? (2009)
Equity Trustees - Cancer Research Trust, $6,600

SCHOLARSHIPS, AWARDS AND PROMOTIONS

Professor Gail Risbridger

- Monash University Vice Chancellor Special Commendation for Postgraduate Supervision

Dr Renea Taylor

- Poster prize, inaugural Ludwig Institute for Cancer Research Translational Oncology Conference, Melbourne
- Monash University Travel Grant Award
- Endocrine Society Travel Grant Award

Roxanne Toivanen

- Australian Postgraduate Award Scholarship
- Rotary Club of Canterbury PhD Scholarship
- Monash University Faculty of Medicine, Nursing and Health Sciences Postgraduate Excellence Award

CENTRE FOR **WOMEN'S HEALTH RESEARCH**

Dr Caroline Gargett, Prof Euan Wallace (Clinical Director), Prof Peter Rogers (Centre Director), Dr Jane Girling

Researchers in the Centre for Women's Health Research work on a wide range of diseases and conditions that affect women, including endometriosis, pre-term birth, infertility and reproductive cancers. Researchers also undertake more fundamental studies on biological processes such as angiogenesis, stem cell differentiation and synchrotron radiotherapy for cancer.

The Centre's funding success in 2009 was the highlight of its tenth anniversary year. Researchers in the Centre were successful in eight out of ten NHRMC project grant applications, and overall gained more than $5.35 million in new research funding. The fact that 22 different chief investigators were involved in obtaining this funding reflects the depth of clinical and basic research expertise in the Centre for Women's Health Research.

In addition to the Centre's NHMRC funding successes, Centre Director, Professor Peter Rogers, received $206,500 from the Cancer Council Victoria to continue his work into the use of synchrotron microbeam radiation therapy for cancer patients. Funding secured by Dr Carl Sprung from the Marian & EH Flack Trust and LEW Carty Charitable Fund, as well as Monash Early Career Development awards to Dr Jeff Crosbie and Dr Marina Zaitseva, will expand the research effort in this exciting new area.

Dr Caroline Gargett received a $201,000 grant from the Australian Stem Cell Centre. Collaborating with the CSIRO, Dr Gargett is aiming to develop a tissue engineering device using endometrial stem cells to repair pelvic floor prolapse. This condition commonly occurs due to damage to the pelvic floor tissues during childbirth.

Dr Tu'uhevaha Kaitu'u-Lino showed that science and popular culture can mix, when she was named *Cosmopolitan* magazine's Inspirational Role Model and won the 2009 Fun Fearless Female Woman of the Year. She received the two awards in recognition for her research into the role endometrial stem cells play in problem periods; an issue that affects four million Australian women.

RESEARCH HIGHLIGHTS

Evidence for cancer stem cells in human endometrial carcinoma

Dr Caroline Gargett and her team recently discovered rare populations of adult stem cells in human endometrium, the highly regenerative lining of the uterus. Dr Gargett hypothesised that cancer stem cells (CSCs) may be derived from the endometrial epithelial progenitor cells and may play a key role in the pathogenesis of endometrial carcinoma, the most common gynaecological malignancy in women. This paper reports on the identification of a rare CSC population in human endometrial cancer using similar approaches that identified epithelial progenitor cells in normal endometrium. Rare single cells isolated from 34 endometrial cancer tissues showed characteristic properties of CSCs producing clones of cells at a similar frequency (0.24%) for the different grades of endometrial cancer, which was also similar to that for normal endometrial epithelial cells. Importantly, relatively low numbers of freshly isolated endometrial cancer cells from 8/9 patient samples transplanted into mice generated tumours resembling the parent tumour in architecture and molecular features, including cytokeratin, vimentin, estrogen receptor-α, and progesterone receptor expression, indicating that the transplanted tumour-initiating CSCs differentiated into the cancer cells of the tumour. The study also showed that clonally-derived endometrial cancer cells could be serially subcultured at cloning densities two to four times, expressed the key self-renewal genes BMI-1, NANOG and SOX-2, and that cells freshly isolated from primary tumours could be serially transplanted up to 5 times, demonstrating extensive self renewal, a defining CSC trait. This evidence of rare cells with clonogenic, self-renewing, differentiating and tumorigenic properties suggests a CSC population may be responsible for production of endometrial cancer tumour cells.

Hubbard SA, Friel AM, Kumar B, Zhang L, Rueda BR, Gargett CE (2009) Evidence for cancer stem cells in human endometrial carcinoma. *Cancer Res* 69:8241-8248.

Priorities for endometriosis research: Recommendations from an international consensus workshop

Endometriosis affects an estimated ten percent of women in the reproductive-age group, rising to thirty percent in women with infertility. Women with endometriosis endure a significant impact on their general physical, mental and social well being. There is no known cure, and most current medical treatments are not suitable long term due to their side-effect profiles. Endometriosis has an estimated annual cost in the USA of $18.8 to $22 billion (2002 figures), when direct and indirect costs including lost work productivity are combined. Although endometriosis was first described over 100 years ago, current knowledge of its pathogenesis, spontaneous evolution, and the pathophysiology of the related infertility and pelvic pain, remain unclear. Further, research into these problems has been limited and is significantly underfunded in many, if not all countries.

To commence addressing these issues, a World Endometriosis Society and World Endometriosis Research Foundation consensus workshop was held following the 10th World Congress on Endometriosis (WCE) in Melbourne in March 2008. The workshop was chaired by

Professor Peter Rogers and was tasked with establishing recommendations for priorities in endometriosis research. The format for the meeting was for a number of sessions covering different groups of endometriosis-related topics with different moderators responsible for each session. Each moderator was also asked to monitor relevant talks and posters at the preceding WCE meeting and include new findings and ideas in their session. The primary outcome for the workshop was to produce a set of recommendations that could be submitted for publication to the international peer-reviewed journal Reproductive Sciences. A total of 25 recommendations for research were developed and grouped under five subheadings: diagnosis, classification and prognosis, treatment and outcome, epidemiology and pathophysiology. It is hoped that this international research priorities statement will act as both a guide and a stimulus to the international research community, and the many funding agencies that may provide support for endometriosis research. A revised and updated set of research priorities which builds on this document, and progress as a result of our efforts, will be developed in conjunction with the 11th World Congress on Endometriosis to be held from 4 to 7 September 2011, in Montpellier, France.

Rogers PA, D'Hooghe TM, Fazleabas A, Gargett CE, Giudice LC, Montgomery GW, Rombauts L, Salamonsen LA, Zondervan KT (2009) Priorities for endometriosis research: recommendations from an international consensus workshop. *Reprod Sci* 16:335-346.

GRANTS AWARDED IN 2009

NHMRC Project Grants

S Miller, G Jenkin, E Wallace
Treatment of cerebral palsy: an experimental approach (2010-2012)
$568,500

L Parry, M Tare, J Girling, M Wlodek
Mechanisms of impaired uterine vascularisation in early pregnancy (2010-2012)
$550,050

P Rogers, R Lewis, C Sprung
Optimising synchrotron microbeam radiation therapy for cancer treatment (2010-2012)
$625,625

P Rogers, B Vollenhoven
Fibroblast function in uterine leiomyoma (2010-2012)
$505,650

J Girling, M Hedger, D de Kretser, P Rogers
Novel roles for follistatin in reproductive biology (2010-2012)
$591,500

H Teede, B Strauss, J Zierath, N Stepto, J Cameron
Insulin resistance in polycystic ovary syndrome and the role of skeletal muscle and adipose tissue (2010-2011)
$404,750

S Tong, TG Johns
Development of novel medical therapies to cure ectopic pregnancies (2010-2012)
$504,250

E Wallace, G Jenkin, T Moss, S Miller, A Veldman
Preventing preterm lung disease - a cell therapy approach (2010-2012)
$444,189

NHMRC Equipment Grant

R Andrews, C Gargett, I Harper, M Hickey, S Jackson, D Jans, B Jenkins, K Loveland, U Manuelpillai, R Medcalf, DN Watkins, E Williams
Establishment of MMI advanced microscopy platforms for live cell and intravital imaging (2009)
$220,000

NHMRC Medical Postgraduate Research Scholarship

R Hodges
Treatment of lung disease in premature babies with human amnion cells (2009-2011)
$97,884

Cancer Council Victoria Venture Grant

P Rogers, D Blakey, R Lewis, I Svarb, BRG Williams
The biological effects of synchrotron microbeam radiation therapy on normal and tumour tissues (2009-2010)
$206,500

Australian Stem Cell Centre

C Gargett, S Edwards, K McLean, A Rosamilia, J Werkmeister
Investigating adult stem cells for regenerating the pelvic floor (2010-2011)
$201,225

RANZCOG (Royal Australian and New Zealand College of Obstetricians and Gynaecologists) Research Foundation

R Hodges
Prevention of preterm lung disease by human amnion cells (2009-2010)
Glyn White Research Fellowship, $60,000

Faculty of Medicine, Nursing and Health Sciences Early Career Development Grants 2010

J Crosbie
Bio-dosimetry to enable synchrotron microbeam radiation therapy (mrt) for cancer (2010)
$35,000

M Zaitseva
Differences in toll-like receptor signalling between normal and cancer cells after conventional and microbeam radiation therapy (2010)
$35,000

Philanthropic grants

D Healy
Analysis of perinatal outcomes for mothers and singleton babies after Assisted Reproductive Technology (ART) (2009-2011)
BUPA (British United Provident) Foundation, $259,949

C Sprung
Severe radiotherapy reactions: genome-wide exon array analysis and early radiation response (2009)
LEW Carty Charitable Fund, $31,059

C Sprung
Synchrotron microbeam radiotherapy for cancer treatment using cultured cells (2009)
Marian & EH Flack Trust, $30,000

P Rogers
Gene expression profiling of human breast tumours to identify prognostic indicators for successful response to chemotherapy (2009)
Monash Oncology Research Institute $25,000

S Tong
Development of a novel medical therapy to treat ectopic pregnancies (2009)
Helen Macpherson Smith Trust, $36,000

SCHOLARSHIPS, AWARDS AND PROMOTIONS

Dr Tu'uhevaha Kaitu'u-Lino
- RANZCOG Arthur Wilson Memorial Scholarship
- Winner, Cosmopolitan Magazine Fun Fearless Female Award

Dr Tamara Yawno
- New Investigator Travel Award, 5th International Meeting Steroids and Nervous System

Ryan Hodges
- Winner, RANZCOG Organon Women's Health Care Prize

Fifie Mogami
- Cancer Council Vacation Studentship

Dr Rebecca Lim
- First prize, MIMR Scientific Retreat Poster Presentation

Hong Nguyen
- Winner, Southern Health Research Week Poster Award, Women's Health Research

Wan Tinn Teh
- RANZCOG Luke Proposch Perinatal Research Scholarship

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 2009, Andrology Australia's program of activities focused on furthering strategic collaborations and the work of its expert reference working groups in developing research capacity and educational initiatives in men's health.

New working groups were established in 2009 to further build capacity through shared knowledge and research. The Social Determinants Reference group, as part of the Men's Health Australia Longitudinal Study, and the Culturally and Linguistically Diverse (CALD) Reference Committee aim to identify priority educational needs for men and health professionals from CALD communities. Building on the Andrology Australia professional education program, a Practice Nurse Education Reference Group was also established to develop education programs specifically for the needs of practice nurses.

Other key highlights for 2009 included the Andrology Australia '*The Healthy Male*' forum (Gold Coast, Queensland), which provided an overview of the latest developments and understanding in men's health. The forum brought together more than 100 Andrology Australia associates to discuss the issues facing both younger and older men, associations between social factors and health behaviours, and the latest men's health research and medical interventions. The forum highlighted strong themes with a need for interdisciplinary care, including linkages between reproductive health problems and other chronic diseases.

The launch of an annual Andrology Australia 'Merv's Have a Crack Day' cricket fundraising event was a further highlight of the year. The event was established as a means to enhance the program's capacity to provide a range of community men's health resources and programs at no cost.

Community education continued with Ambassador Merv Hughes speaking at a number of men's health events in regional areas across Australia. The growing community awareness of Andrology Australia was evident with increasing usage of the website (www.andrologyaustralia.org) with, on average, more than 1.2 million hits, 50,000 visitors and approximately 25,000 downloads per month in 2009.

Visit www.andrologyaustralia.org for more information.

EDUCATION

VISITING SPEAKERS 2009

MIMR's Seminar Series was proudly supported by DKSH.

Dr Erica Sloan
UCLA Semel Institute of Neuroscience and Human Behaviour, Los Angeles, USA
Neural regulation of cancer and HIV (4/2/09)

Professor Graham Jenkin
Deputy Director, and Head, Fetal Development, Stem Cells and Differential Group, Monash Immunology and Stem Cell Laboratories, Monash University
Stem cells, fetal growth restriction and perinatal well-being (2/3/09)

Associate Professor Laura Bennet
Department of Physiology, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand
The preterm fetus and newborn: challenges for the clinician and scientist (4/3/09)

Dr Dino A Giussani
Reader in Developmental Cardiovascular Physiology & Medicine, Department of Physiology, Development & Neurosciences, University of Cambridge, USA
Heart Disease Link to Oxygen in the Womb (5/3/09)

Professor Peter Currie
Deputy Director, Head, Regenerative Biology Unit, Australian Regenerative Medicine Institute Monash University
Modelling muscle development, disease and regeneration in zebra fish (5/3/09)

Associate Professor Mary Wlodek
Head, Fetal, Postnatal and Adult Physiology and Disease Laboratory, Department of Physiology; Associate Dean, Melbourne School of Graduate Research, The University of Melbourne
Solving the developmental programming puzzle - windows of opportunity for growth restricted offspring (9/3/09)

Dr Ludwig Gortner, MD
Professor of Paediatrics, Clinics of Paediatrics and Adolescent Medicine, University of the Saarland, Germany
Intrauterine growth restriction: a risk factor only during the perinatal period? (11/3/09)

Dr Andreas Muller
Honorary Fellow, Cancer Genomics and Biochemistry Group, Peter MacCallum Cancer Centre
Inhibition of siah ubiquitin ligases slows cancer progression (12/3/09)

Professor Leigh Murphy
Department of Biochemistry and Medical Genetics; Chair, Breast Cancer Research Group, The University of Manitoba, Canada
Oestrogen receptor profiling in human breast cancer - towards better prediction of endocrine therapy response (17/3/09)

Associate Professor Damien Jolley
Monash Institute of Health Services Research, School of Public Health & Preventive Medicine, Monash University
Visualising variables validly (26/3/09)

Professor Stefan Rose-John
Department of Biochemistry, Christian-Albrechts-Universitat zu Kiel Medical School, Germany
Analysis of the role of IL-6 trans-signaling and the metalloproteinase ADAM17 in inflammation and cancer (2/4/09)

Dr Michael A Cahill
Lecturer in Biochemistry, School of Biomedical Sciences, Charles Sturt University, NSW
Towards the role(s) of the putative membrane steroid receptor PGRMC1 in breast cancer (8/4/09)

Professor Louis Guillette Jr
Department of Zoology, University of Florida, USA
Environmental contaminants and the resulting reproductive and endocrine disruption (8/4/09)

Dr Elizabeth Guillette
Department of Anthropology, University of Florida, USA
Future parenthood: threats from manufactured chemicals (9/4/09)

Professor Justin St John
Clinical Sciences Research Institute, University of Warwick, University Hospital, Coventry, UK
The continuous recycling of the mitochondrial genome from one generation to the next - is intervention necessary when applying more sophisticated reproductive strategies? (24/4/09)

Professor Brandon Wainwright
Institute for Molecular Bioscience, University of Queensland, Queensland
The hedgehog pathway in stem cell regulation and tumourigenesis (30/4/09)

Dr John Silke
Department of Biochemistry, LaTrobe University
RINGing in the changes, new insights and old misconceptions in TNF signalling (21/5/09)

Associate Professor Ian Davis
Medical Oncologist, Ludwig Institute for Cancer Research, Austin Hospital
Cancer immunotherapy: recognise it, tolerate it or reject it?(28/5/09)

Professor Peter Leedman
Laboratory for Cancer Medicine, Western Australian Institute of Medical Research, WA
MicroRNAs, nuclear receptors and cancer (4/6/09)

Dr Grant Drummond
Vascular Pharmacology and Immunobiology Group, Department of Pharmacology, Monash University
NADPH oxidases as novel therapeutic targets in vascular disease (7/7/09)

Dr Dharani Hapangama
Senior Lecturer/Consultant in Obstetrics & Gynaecology, Reproductive and Developmental Medicine, University of Liverpool, UK
Endometrium, endometriosis and telomerase (4/8/09)

Professor Jonathan Morris
Research Group Leader, Perinatal Medicine, Kolling Institute of Medical Research, NSW
Understanding the immune regulation of pregnancy and its Implications for pre-eclampsia and autoimmunity (11/8/09)

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

VISITING SPEAKERS 2009 (CONTINUED)

Dr Gendie Lash
School of Surgical and Reproductive Sciences, University of Newcastle upon Tyne, UK
A functional role for uNK cells in early pregnancy decidua (13/10/09)

Emeritus Professor Gordon Campbell
University of Queensland, QLD
Tissue engineering of hollow smooth muscle organs (19/11/09)

Professor Julie Campbell
Research Professor, University of Queensland; Director, Wesley Research Institute, Wesley Hospital, QLD
Diverse origins of smooth muscle during repair (19/11/09)

Dr Keren Abberton
Senior Research Officer, Bernard O'Brien Institute of Microsurgery
Adipogenesis and inflammatory interactions: the role of inflammation in engineering adipose tissue (1/12/09)

EDUCATION PROGRAM IN REPRODUCTION AND DEVELOPMENT

2009 marked twenty-one years since the Education Program in Reproduction and Development (EPRD) began running postgraduate courses. As the Program continues to expand, 2009 also marked the beginning of the Masters of Clinical Embryology (MCE) off-campus course. These milestones recognise the long-term relevance of this Program in postgraduate education and the continued student interest in reproduction and development.

In 2009, the strategic priorities for EPRD were to continue improvements to the course structures and administration, to gain Honours equivalence for our courses and to launch, at the national level, an off-campus version of the MCE course. Expanded and improved laboratory facilities and equipment upgrades throughout the year continued to provide the Program with a strong competitive edge nationally and internationally.

EPRD courses were again a popular choice for graduates in 2009. Twenty-two students from Australia and ten other countries enrolled in the MCE course. Seventeen graduates are now employed in IVF laboratories in around the world, three are enrolled in research degrees and one is pursuing a career in reproductive medicine. Eleven students completed the Graduate Diploma in Reproductive Sciences and three students completed the Master of Reproductive Sciences degree.

The Program continued to develop strong, international collaborations. A delegation, including specialist trainees, from Gadjah Mada University's Faculty of Medicine visited

EPRD. The trainees took part in specialist infertility training with staff from the EPRD and collaborating organisations. In September, the Dean of the Faculty of Medicine, Padjajaran University, Indonesia visited to develop further collaborations in assisted reproductive technologies and infertility management training. EPRD staff also supported conferences and research activities. Dr Sally Catt conducted three vitrification workshops in Melbourne and Kuala Lumpur. Staff also presented at meetings around Australia and in Vietnam, China and Argentina.

The Program's activities were again supported by MIMR, Prince Henry's Institute, Monash Medical Centre, Monash University Faculty of Medicine, Nursing and Health Sciences. Staff from Monash IVF, Melbourne IVF, the University of Melbourne, Family Planning Victoria, Zoos Victoria, Genetics Australia, Melbourne Aquarium, Victorian Assisted Reproductive Treatment Authority and Sydney IVF were also involved in teaching and providing work placement opportunities for MCE students during the year. Expanded and improved laboratory facilities and important upgrades in laboratory equipment during the year continued to provide the programs with a strong competitive edge, both nationally and internationally.

MIMR POSTGRADUATE COMMITTEE

The MIMR Postgraduate Committee provides support and mentoring for MIMR students and their supervisors, with the aim of making the progress of each student towards the completion of their degree as seamless as possible. The committee, made up of representatives from each Centre, meets monthly to review student progress and deal with any issues arising within students' studies.

In addition to organising the University's formal postgraduate requirements, social events are also coordinated through the Postgraduate Committee. The welcome barbeque in March and the Postgraduate Symposium for third and fourth-year students create a nurturing, stimulating and fun environment for students.

A postgraduate information section on the MIMR intranet was launched in 2009 to provide a suite of resources for early-career researchers. An accompanying postgraduate skills program was implemented, which included workshops on writing scientific abstracts, designing scientific posters, scientific presentations and effective job applications.

COMMUNITY EDUCATION

The Institute is committed to encouraging secondary school students with a passion for medical research. To nurture the scientists of tomorrow, the Postgraduate Committee coordinates a work experience program for students in years 10 to 12. In 2009, 14 students from metropolitan and regional high schools undertook work experience at MIMR. Students spent time in each of the Institute's main research Centres and technical facilities, and had a valuable insight into a medical researcher's world.

STUDENT OPEN DAY

MIMR's annual Student Open Day promotes the diverse range of research opportunities available to prospective students. Tours of the Institute's research centres and core facilities were conducted by current MIMR students, and were nominated as a highlight by the visiting students. Information stands in the de Kretser Concourse provided the opportunity for one-on-one interactions between prospective students and current trainees from each Centre.

STUDENT SYMPOSIUM

The annual Student Symposium provides third and fourth-year PhD students with the opportunity to present their research to their peers and senior scientists within MIMR. Each student has 20 minutes to discuss their work, and to answer questions from the audience. It is an invaluable lesson in scientific presentation skills for these early-career scientists.

The winners of the student prizes kindly donated by Invitrogen and Biocomm2 were:

Third-year presentations

1st: Ka Yee Fung

2nd: Tali Lang

3rd: Corey Heffernan

Fourth-year presentations

1st: Nicole Witcomb

2nd: Pollyana Tat

3rd: Scott Sands

Team player awards

Alex Wilding

Sarah Wilkinson

Ritchie Centre Acting Director, Dr Philip Berger (far left) and Adjunct Professor, Prof Adrian Walker (far right) with the 2009 Ritchie Centre Graduates: Dr Brad Edwards, Dr Heidi Richardson, Dr Joel Yang, Dr Nicole Witcombe, Dr Susan Feng.

2009 GRADUATES

Congratulations to all students who completed their studies in 2009.

PhD

Priscila Cassaglia, Ritchie Centre for Baby Health Research:
Sympathetic neural control of the cerebral circulation in sleep

Tung-Liang (Tom) Chung, Centre for Reproduction and Development / Centre for Cancer Research:
CD30 receptor: regulation of expression and its role in cultured human embryonic stem cells

Melissa Cooney, Centre for Reproduction and Development:
Characterisation of bovine sperm factor protein PLC zeta and investigation of its role in oocyte activation

Anna Cvrljevic, Centre for Reproduction and Development / La Trobe University:
Activation of Src family kinases in human derived glioma cell lines induces mitochondrial localisation of the De2-7 EGFR

Jonathan Daly, Centre for Reproduction and Development:
The use of assisted reproductive technology in elasmobranch fish: potential for helping the grey nurse shark

Kathryn Davidson, Centre for Reproduction and Development:
A study of Wnt3a protein function in the maintenance, survival, and proliferation of human embryonic stem cells and their progenitors

Vinali Dias, Centre for Reproduction and Development:
TGFB superfamily signaling in germline specification and germ cell tumors

Jacqueline Donoghue, Centre for Women's Health Research:
Molecular regulation of uterine lymphangiogenesis

Brad Edwards, Ritchie Centre for Baby Health Research:
Mechanisms underlying periodic breathing during development: insights from loop gain

Susan Ying Shan Feng, Ritchie Centre for Baby Health Research:
Effects of perinatal infection on the cerebral circulation

Mei Ling Lim, Centre for Reproduction and Development:
The effect of epigenetic modification on the generation of pluripotent and reprogrammed somatic cells

Heidi Richardson, Ritchie Centre for Baby Health Research:
Infant arousal processes: implications for sudden infant death syndrome

Kyle Upton, Centre for Reproduction and Development:
Analysis of changes in the epigenetic state of reprogrammed somatic cells

Brett Verstak, Centre for Immunity and Infectious Diseases:
Characterisation of the interaction between Mal and TRAF6 in Toll-like receptor signalling

Nicole Witcombe, Ritchie Centre for Baby Health Research:
Development of cardiovascular control during sleep in human infants after preterm birth

Flora Yuen-Wah Wong, Ritchie Centre for Baby Health Research:
New bedside techniques utilising near infrared spectroscopy in preterm infants

Joel Shao-Chung Yang, Ritchie Centre for Baby Health Research:
Assessment of sleep quality in children with sleep disordered breathing: evaluation of EEG spectral analysis

Natasha Zamudio, Centre for Reproduction and Development:
Epigenetic regulation and male fertility

PhDSci

Jeffrey Crosbie, Centre for Women's Health Research / Monash University Department of Physics

Bachelor of Science (Honours)

Lori Turner, Centre for Innate Immunity and Infectious Diseases:
The immunomodulatory roles of Helicobacter pylori outer membrane vesicles.

Bachelor of Biomedical Science (Honours)

Upeksha Chandrasiri, Centre for Urological Research
The therapeutic use of an estrogen receptor beta (Erß) selective agonist in androgen independent prostate cancer

Samuel Forster, Centre for Innate Immunity and Infectious Diseases
Biological and computational annotation of the Type 1 interferon signalling pathway.

Simon Preston, Centre for Innate Immunity and Infectious Diseases
The role of Lipocalin 2 in antimicrobial responses to helicobater pylori infection.

Yue (Vicky) Xin, Centre for Cancer Research
The role of PKR in the activation of NF-κB activation

Bachelor of Biomedical Science

Susie Broughton, Centre for Women's Health Research:
Quality of life of Ethiopian women with ileal conduits following obstetric injury

Kristina Herlambang, Education Program in Reproduction and Development:
Investigating mitochondrial function and oxygen utilization in frozen-thawed compared to fresh mouse blastocysts

Dini Irawan, Centre for Cancer Research
Characterization of the anti-apoptotic pathway regulated by CCAAT/enhancer binding protein beta (C/EBPB) in Wilms tumor cells

Peter Morris, Centre for Cancer Research:
The role of hedgehog signalling in the repair of small intestinal epithelium

Patricia Vosdoganes, Centre for Women's Health Research:
Investigating the role of human amniotic epithelial cells in the treatment of inflammation-induced preterm lung injury

EDUCATION PROGRAM IN REPRODUCTION AND DEVELOPMENT GRADUATES

Master of Clinical Embryology

Persiyasaral Arokiam

Parveen Mahaboob Basha

Nyssa Brown

Mathew Eyre

Hanna Genee

Hadeel Khayat

Hui Ling Carolyn Koon

Vidhu Krishnan

Yanhe Liu

Meidona Milla

Anjali Ann Ninan

Panharith Ouk

Kiratikorn Punyatrong

Normalina Sandora

Ramya Sundaram

Kurshith Thameen

Undraa Tumurbaatar

Sharona Ungar

Bich Thuy Vu

Heba Zahid

Graduate Diploma in Reproductive Sciences

Penelope Bradshaw

Sonari Fernando

Hayley Fisher-Stamp

Chloe Goodie

Seungmin Ham

Hui Ling Koon

Afsaneh Mehrabkhani

Vivek Navneet

Daniel Petkovski

Stephanie Sullivan

SUPPORTING OUR RESEARCH

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

MONASH HEALTH TRANSLATION PRECINCT CORE FACILITIES

The Monash Health Translation Precinct (MHTP) brings together researchers from MIMR, Monash University and Prince Henry's Institute, with clinicians and patients from Southern Health's Monash Medical Centre. Close collaboration increases the impact of research through translation of laboratory findings into improved clinical treatments.

Precinct members share a number of resources and advanced facilities that further research capacity. These core facilities are managed by MIMR staff and scientists. Throughout 2009, all areas within the Core Facilities cluster continued to expand and improve their services.

Two new instruments were introduced during the year. The DeltaVision microscope allows for super-resolution, live-cell imaging and the Roche xCELLigence allows researchers to investigate real-time cellular events over a period of days, without the incorporation of expensive labels.

Gandel Charitable Trust Sequencing Centre

The Gandel Charitable Trust Sequencing Centre supports medical researchers throughout Victoria through its provision of a NATA*-accredited DNA sequencing service. The Centre maintains the highest quality of service delivery while initiating innovative applications of the technology within the healthcare sector. DNA sequencing is the technique used to determine the exact order of bases within DNA. It is used to understand gene structure and is an essential platform technology underpinning a majority of medical research programs currently undertaken within the MHTP. DNA sequencing is also a critical diagnostic method for a number of inherited diseases.

In 2009, the Centre celebrated its tenth anniversary. Originally named the Wellcome Trust Sequencing Centre, the facility was renamed in 2006 in recognition of a generous grant from the Gandel Charitable Trust enabling purchase of the current 16 capillary 3130xl Genetic Analyser used within the facility. Since then, the Sequencing Centre has introduced complementary genomic services, including fragment analysis, gene expression and DNA, RNA and protein analysis. Furthermore, the Sequencing Centre has been able to expand its client service base to more than 500 research and clinical personnel throughout Victoria (Figure 1).

*NATA is a government-endorsed authority that provides independent assurance of technical competence through assessment against Australian and International operating standards.

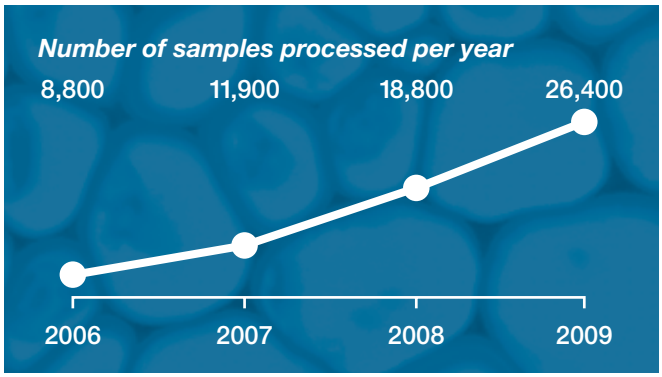


Figure 1: DNA Sequencing samples processed by the centre have increased by an average of 30% each year over the previous three years.

Monash High Content Screening Facility

The Monash High Content Screening Facility core infrastructure includes a ThermoFisher ArrayScan Instrument, whole genome RNAi libraries and liquid handling robotics.

The ArrayScan is an automated microscope that enables capture and quantitative analysis of cell biology experiments. In addition to deriving quantitative data from previously empirical experimental approaches, the use of automation allows more extensive experimental approaches. Thus, this instrument has been in increasing demand during 2009 by many of the Precinct researchers as suitable assays are adapted and/or developed to be used on this platform. External users now include CSIRO, Prince Henry's Institute and the Monash Immunology and Stem Cell Laboratories.

The whole genome RNAi libraries enable researchers to individually inhibit every gene in the human or mouse repertoire and measure changes in specific cell functions. Throughout the year, development and optimisation of assays to identify new genes that contribute to important biological processes continued. These include assays to identify novel genes involved in cancer development and drug resistance, new mechanisms that could be used to enhance (or inhibit) stem cell differentiation into specific lineages and innovative approaches to inhibit infection. In the next year it is anticipated that these assays will be optimised and used in whole genome screens.

Flow Cytometry

The Flow Cytometry Facility provides quality research and clinical services to all staff and students within the MHTP and to the wider research community. Flow cytometry is a laser-based technology that provides simultaneous measurement of multiple cellular parameters at very high speeds, resulting in rich datasets in minimum time. The facility operates two cell sorters and two cell analysers that are used by over 100 clients to further research into a variety of fields, including immunology and auto-immunity, stem cells, cancer research, developmental biology, cardiology and diagnostic pathology.

2009 saw the introduction of a new online booking system, which provides users with the flexibility to check instrument availability and book time on the instruments over the internet. Additionally, the facility has purchased a dedicated computer for offline data analysis and a license of the popular flow cytometry analysis software FlowJo.

Monash Medical Centre Animal Facility

The first half of 2009 saw Monash Medical Centre Animal Facility (MMCAF) outfit its expanded SPF areas with new colonies of mice and the holding capacity for experimental SPF mice. Research into embryo rederivation of various mouse lines into our High Barrier SPF commenced.

Carlie Tobias joined MMCAF as the facility's Conventional Supervisor, and some casual staff were transferred to full time positions.

SUPPORTING OUR RESEARCH

Rod Wealands, Chief Operating Officer

Micro Imaging

The Monash Micro Imaging Facility provides consultation, training, reagents and imaging technologies, encompassing timelapse molecular fluorescence imaging as well as sophisticated 4D reconstruction and multiphoton imaging techniques.

In 2009, the facility trained and supported over 60 staff and students, with instrument usages totalling over 2600 hours. Through a joint NHMRC equipment grant between Monash Micro Imaging (Monash University), Southern Clinical School (Monash University) and MIMR, a brand new laser scanning confocal microscope was installed and commissioned on site, enabling researchers to investigate and manipulate disease and biological characteristics inside living cells for Precinct researchers.

Histology

The Histology Facility provides a range of paraffin and resin histological services to researchers in the MHTP and external clients.

An online job submission and booking service was implemented in 2009, making histology services more accessible to internal clients. Closer ties with Monash University's Histological Laboratory Service has led to a broader range of services available, including sledge microtomes for larger samples, vacuum processing for dense tissue such as bone, and a range of special stains.

Collaborations with other core facilities, such as the Micro Imaging Facility, has allowed for greater tailoring to individual requirements.

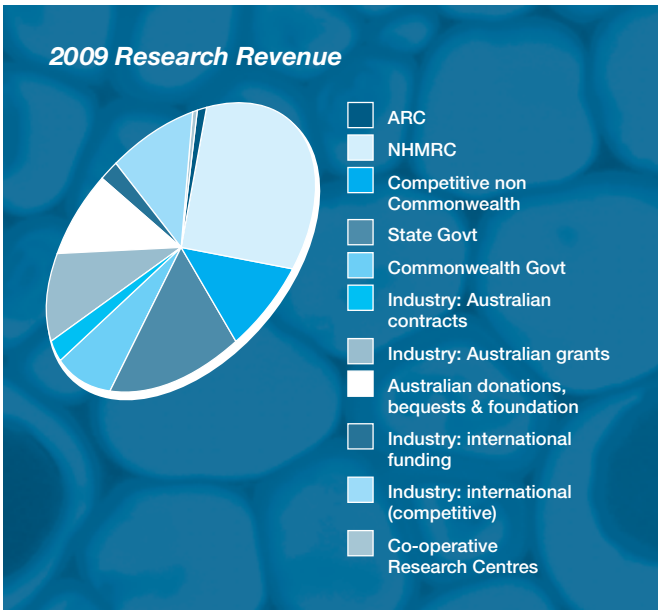
CHIEF OPERATING OFFICER REPORT

2009 was another incredibly successful year for MIMR. With a consistent core admin staffing profile we were able to deliver high quality service and support to our researchers.

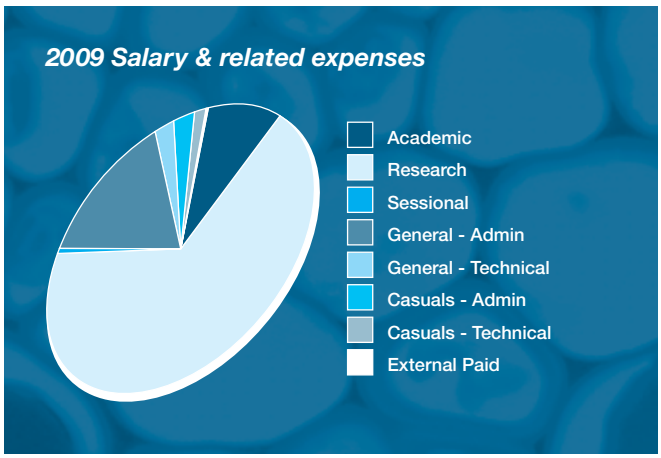
Changes were implemented as a result of the external review of administrative services in 2008. Additional resourcing in the Finance, Human Resources and Logistics teams will ensure high standards of service are maintained. The expansion of the administrative team was ideal preparation for the additional work effort required once the MHTP building project commences in 2010.

With a total annual turnover of just under $22 million dollars our team continues to support an ever growing number of researchers and support staff with professionalism and integrity. Graph (1) illustrates all sources of research revenue in 2009. Almost 50% of the Institute's research revenue was generated through competitive grant funding, demonstrating the strength of MIMR's research. As graph (2) shows, the Institute's researchers account for 75% of salary expenses, signifying the investment placed in our researchers.

Rod Wealands
Chief Operating Officer



Graph 1.



Graph 2.

SUPPORTING OUR RESEARCH

Dr Rocco Iannello, Senior Business Development Manager

HUMAN RESOURCES

The Institute's Human Resources (HR) team focuses on continuous improvement of HR services to attract, retain and support the talented and committed staff and students who contribute to the Institute's strong research programs.

In March, the Institute's HR Advisor, Ms Lisle Williams, left on a period of maternity leave. Her replacement, Ms Tali Nassau, readily stepped in to the position and continued to provide staff and students support and advice on a broad range of HR issues.

Although staff numbers remained stable throughout 2009, a strong demand for staff administration continued. More than 200 new appointments and contract renewals were coordinated throughout the year.

Research Centres continued to attract an increased number of international appointments, visitors, honoraries and affiliation, which contributed to the constant strengthening of the Institute's innovative research environment.

LOGISTICS

The Logistics team looks after the day-to-day running of the Institute, and support the needs of researchers and staff. Primary tasks include asset management, laboratory moves, inward and outward goods, contracts, purchasing, mail, and general maintenance throughout the Institute's two buildings.

During 2009, three research groups moved on from MIMR, and one large team arrived. The Logistics team played a pivotal role in supporting the three groups and planning, designing and implementing the refurbishment of laboratory and office space.

Work began on a new SAP warehousing module, which, when implemented in 2010, will bring considerable savings in the budget and reporting.

INDUSTRY ENGAGEMENT AND COMMERCIALISATION

The basic research undertaken at MIMR has always formed the foundation for relevant and innovative translational activities, and 2009 was no exception. From an industry engagement perspective, relationships were forged with a number of biotech and pharma companies to pursue translational and innovative research, which we hope will lead to beneficial outcomes in the future. The attraction of industry to MIMR has been a combination of both the skill and expertise of our researchers in their respective fields as well as the value and relevance of their research. These areas of research include respiratory disease, regenerative medicine including stem cell biology, oncology including breast cancer, prostate cancer, lung and brain, diabetes, bio imaging, immunity and infection.

2009 saw an increased level of industry engagement and funds generated from these activities. In terms of innovation, MIMR continued to impact in this area. This can be measured by the number of invention disclosures being filed, as well as continued development of research programs, of which there are a number of patent applications currently undergoing examination. All of MIMR's protected intellectual property has generated industry interest and are based around important clinical areas such as cancer, regenerative medicine and women's health.

TECHNOLOGY SERVICES GROUP, SOUTHERN REGIONAL

The Technology Services Group, Southern Regional, provides information technology services and support to staff and students based at MIMR, Prince Henry's Institute and Monash University Faculty of Medicine, Nursing and Health Sciences. In 2009, the group delivered technology services that not only supported the business, but introduced innovation and development, to ensure the future needs of all users.

Information and Communications Technology (ICT) delivery was strengthened in 2009 to assist with and support collaborative arrangements, so vitally important in this global environment. The team successfully delivered effective and efficient services in 2009, as measured by the feedback survey with a 96% approval rating.

We are proud to assist with ICT in a way that allows the core business to function without a focus on ICT and its delivery.

OCCUPATIONAL HEALTH, SAFETY AND ENVIRONMENT

Occupational Health, Safety and Environment (OHSE) is a critical part of MIMR's research and management activities. The Institute's OHSE Manager, Ms Ganeema Tokhi, oversees a range of programs which aim to continually improving health, safety and environmental standards; to minimise the risk of injury and to minimise the risk of harm to the environment.

In 2009, an audit was conducted by external auditors SAI Global to assess the compliance with the University and Victorian OHS standards and legislative requirements. Key findings from the audit report included:

- The OHS management system is robust and widely applied across the Institute with a strong management and staff commitment, in compliance with the requirements of OHS standards.
- No major injuries were noted within the last 12 months.
- Risk assessments were completed for the majority of activities.
- Self assessment audit was completed and identified, issues were followed up for completion and were recorded.
- Accidents and hazards were reported and investigated. Corrective and preventative actions were implemented.
- Workplace inspections were completed as per required schedule.

Institute Environment Program

Delivery of Green Office programs continued throughout 2009. With the assistance of a dedicated team of Green Officers, the Institute is leading its way in the management and reduction of waste by recycling, reducing and re-using material such as paper, cardboard and plastics. In addition, fresh fruit is provided daily to staff and students in lunch rooms.

SUPPORTING OUR RESEARCH

Speakers at the Kaarene Fitzgerald Lecture: Dr Stephanie Yiallourou, Dr Nicole Witcombe, Prof Caroline Blackwell, Dr Heidi Richardson

FUNDRAISING, MARKETING AND COMMUNICATIONS

Community and Philanthropic Support

MIMR is fortunate to have many generous supporters and advocates, including individuals, philanthropic trusts and foundations, and corporate supporters and business leaders. Philanthropy plays a vital role at MIMR, supporting projects that often would not otherwise be funded. We would like to extend our sincere thanks to all our loyal supporters who have funded us this year and continue to help us achieve our vision.

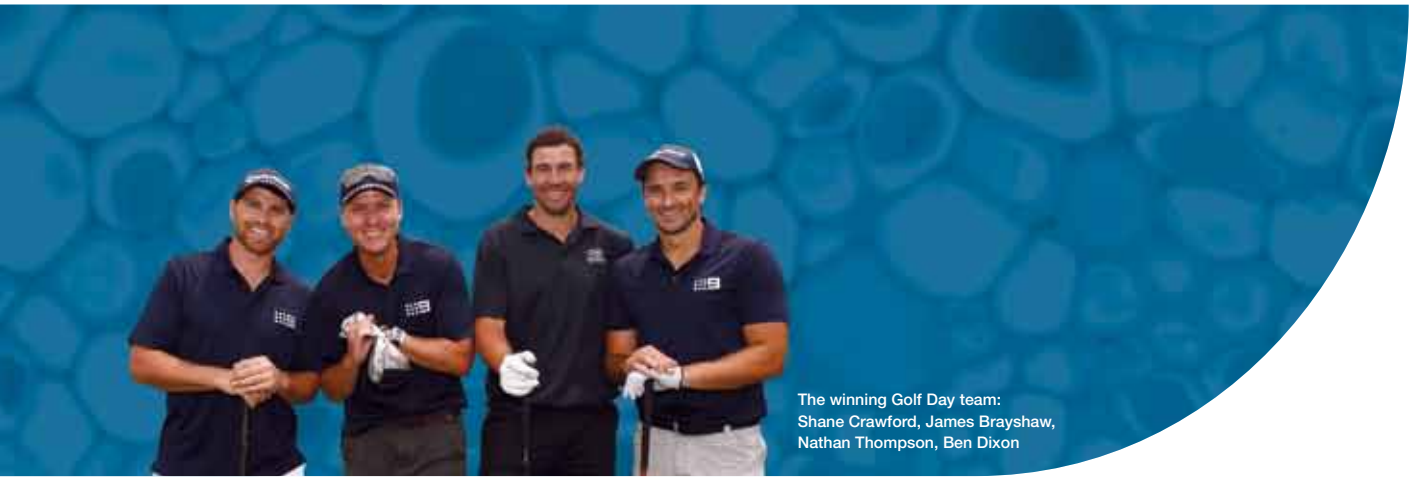
Patrons Club and WISE

The Patrons Club and WISE (Women in Scientific Excellence) play an important role in the Institute. Both groups provide members with the opportunity to interact with scientists at MIMR and hear the latest information about their research. In August, an information evening was held for Patrons Club members and friends to hear the latest research and community education programs in men's health. Professor Gail Risbridger and clinical urologist, Associate Professor Mark Frydenberg, talked about current research into prostate disease and the controversy behind PSA screening for prostate cancer. Professor Rob McLachlan, a Director of Andrology Australia, talked to guests about men's increased awareness and interest in accessing information about men's health issues.

Kaarene Fitzgerald Lecture

The annual Kaarene Fitzgerald Lecture honours the outstanding contributions of Kaarene Fitzgerald AC in over 25 years of service to medical research into sudden infant death syndrome (SIDS). Hosted by the Ritche Centre for Baby Health Research, the lecture provides the public, health professionals and researchers with up-to-date research findings on SIDS.

This year, more than 70 community members and scientists heard from internationally recognised SIDS researcher, Professor Caroline Blackwell, Conjoint Professor of Immunology and Microbiology, University of Newcastle. Professor Blackwell presented on the *Role of infection and inflammation on SIDS*. Other speakers included Dr Heidi Richardson, Dr Stephanie Yiallourou and Dr Nicole Witcombe from the Ritchie Centre, who all spoke about their sleep research and its impact on SIDS.



The winning Golf Day team:
Shane Crawford, James Brayshaw,
Nathan Thompson, Ben Dixon

2009 Golf Day

The Ron Evans Golf Day is held each year to honour the life of Ron Evans AM, an outstanding sportsman, businessman and Monash Alumnus, and to raise important funds for bowel cancer research.

This year, 29 teams battled it out at the Royal Melbourne Golf Course for the highly prized Ron Evans Golf Day Perpetual Trophy. The Channel 9 Team, made up of James Brayshaw, Shane Crawford, Ben Dixon and Nathan Thompson were the eventual winners.

The day concluded with dinner and a silent auction. All proceeds from the day support the Ron Evans Cancer Research Fellowship and Scholarship. The Scholarship, introduced in 2009, is awarded to an outstanding PhD student studying bowel cancer. The inaugural recipient was Matthew Thompson. Matthew's research focuses on a gene, ATF3, and its role in the progression of bowel cancer. Dr Sameer Greenall has held the Fellowship since 2008 and continues to make progress in identifying potential therapies to treat bowel cancer.

The Institute is grateful to the Evans family for their ongoing commitment to nurturing up-and-coming scientists and their research into bowel cancer.

Communicating to the Public

The challenge when communicating medical research stories to the general public is to distil a complex scientific story into easily understood language. The Institute's quarterly newsletter, the *MI News*, the Annual Report, brochures and media releases are all written in this style to highlight research breakthroughs and scientists' achievements to the wider community.

Supporters of the Institute can also learn about scientists' work firsthand through the Discovery Tours program. Participants have the opportunity to visit laboratories and hear scientists explain their research and its potential impact on quality of life. It is also an opportunity for tour participants to learn about the funding needs of the scientists. Groups who visited MIMR in 2009 included members of Probus and Rotary Clubs from around Melbourne, students from Saitama Medical University, Japan, and scientists of tomorrow from Bona Vista Primary School in Gippsland.

SUPPORTING OUR RESEARCH

Donors

MIMR is sincerely grateful for the gifts received from individuals, trusts, foundations and organisations during the year. This valuable support assists the Institute to continue its important research.
We acknowledge the following generous supporters.

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PUBLICATIONS

PUBLICATIONS

CENTRE FOR CANCER RESEARCH

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CENTRE FOR INNATE IMMUNITY AND INFECTIOUS DISEASES

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RITCHIE CENTRE

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FINANCIAL REPORT

MONASH INSTITUTE OF MEDICAL RESEARCH
CASH FLOW STATEMENT YEAR TO DATE 31 DECEMBER 2009

Income	
General Revenue	5,799,196*
Other Income	700,070
Commercial Services Income	77,673
Other Fees	20,000
Student Course Fees	823,929
Investment Income	155,151
Non Research Funding	4,324,813
Scholarships & Prizes	73,717
Research Income	10,012,263
	21,986,812
Salaries Expenditure	
All Salary Expenses	14,663,980
	14,663,980
Non Salary Expenses	
Other Expenses	323,112
Financial & Admin Services	412,261
Travel & Related	756,353
Book & Library	61,578
Print & Stationery	326,103
Computer Related	360,312
Communications	378,976
Equipment Related	104,370
Lab & Operating	3,603,007
Student Related	417,938
Motor Vehicle	21,511
Building & Property	285,956
	7,051,477
Capital Expenditure	
Capital Expenditure	609,384
Operating Surplus/Deficit	-338,029

*Includes Victorian Government Operational Infrastructure Support Funding

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