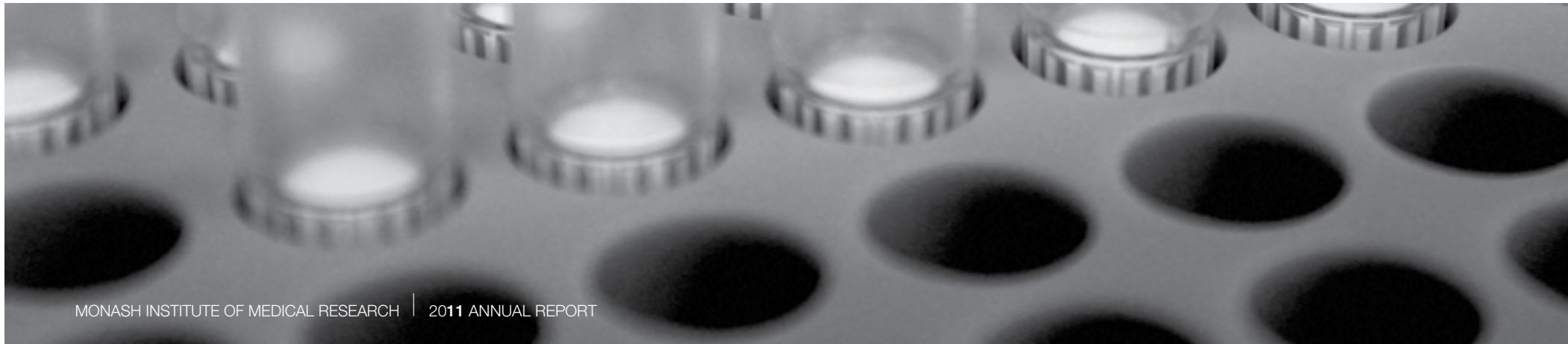
MONASH
INSTITUTE OF
MEDICAL
RESEARCH

2011

ANNUAL REPORT



ABOUT MIMR

Vision

History

Organisational Structure

VISION

As a major medical research institute, MIMR will enhance human health and the quality of life in major research, innovation and discovery in biology, medicine and biotechnology research.

HISTORY

Emeritus Professor David de Kretser AC established the Monash Institute of Reproduction and Development in 1991.

The Institute originally 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 within the Department of Anatomy, Monash University.

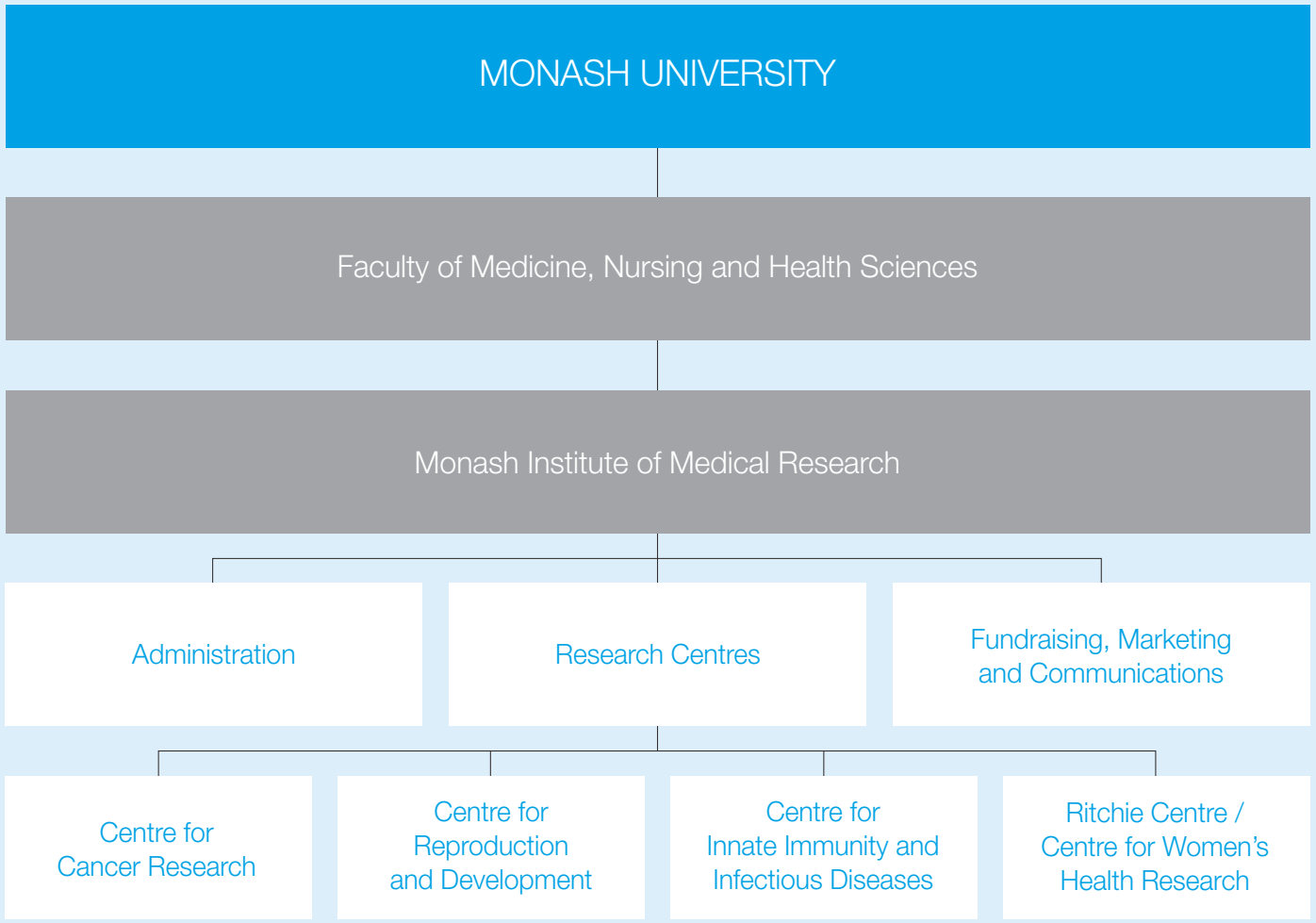
Over the years, the research conducted at the Monash Institute of Reproduction and Development benefitted people worldwide, including infertile young people, premature babies and their families, and men with prostate cancer.

Recognising that its research had evolved beyond reproduction and development, the Institute became the Monash Institute of Medical Research in 2005.

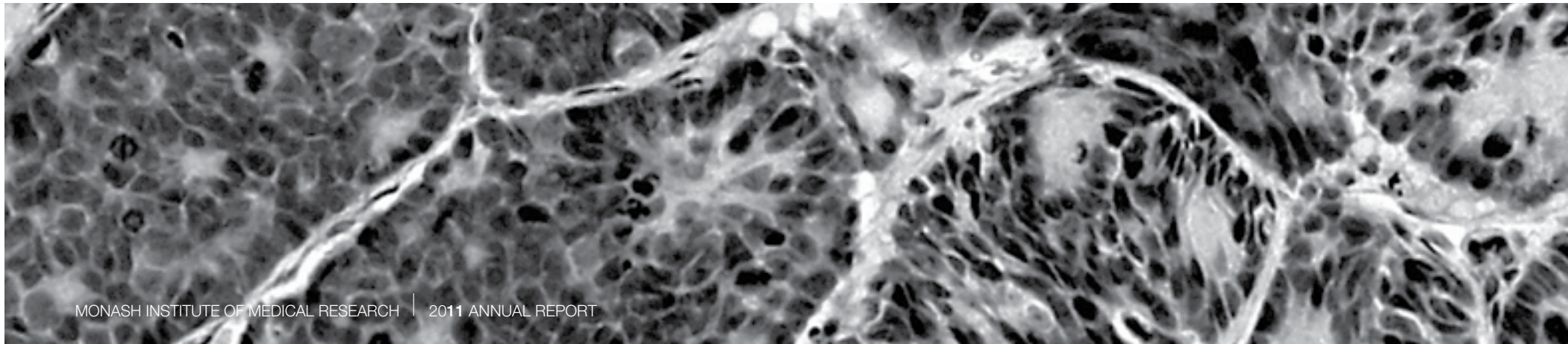
Following Professor de Kretser's retirement in 2005, Professor Bryan Williams, an internationally recognised cancer researcher, commenced as Institute Director.

Today, under Professor Williams' leadership, more than 300 scientists and students carry out research into preterm infant health, cancer, inflammation, infectious diseases, women's and men's health and stem cells.

ORGANISATIONAL STRUCTURE



DIRECTOR'S MESSAGE



DIRECTOR'S MESSAGE

This year marked a major milestone for MIMR – our 20th Anniversary in September. The celebrations included a Scientific Symposium, at which the Chief Scientist for Australia, Professor Ian Chubb, delivered the keynote address.

The Founding Directors of MIMR, Professors David de Kretser and Alan Trounson, attended the Symposium and gave presentations of their research highlights. Our celebrations continued with a dinner for staff and supporters of the Institute, held after the Symposium.

In addition, a reception for MIMR staff was held at Government House in October in recognition of our 20th Anniversary, hosted by the Governor of Victoria, Alex Chernov AO.

The anniversary celebrations provided an opportunity for all staff and students, past and present, to reflect on the significant growth of MIMR over the years and on the scientific achievements of the Institute. There are now more than 300 staff and students conducting research at the Institute, which has developed into a key player in biomedical research.

It is fitting that our Founding Director, Professor David de Kretser AC, returned to MIMR this year, following the end of his term as Governor of Victoria. We are honoured that Professor de Kretser has chosen to return to MIMR to continue his distinguished research career.

The Monash Health Translation Precinct (MHTP) continued to evolve in 2011, with the development of the MHTP Medical Genomics Facility. With the $1.6 million in funding provided by the Australian Cancer Research Foundation (ACRF), the ACRF Centre for Cancer Genomic Medicine was established in 2011.

The new Medical Genomics Facility incorporates the genomic services provided by the ACRF Centre for Cancer Genomic Medicine, The Gandel Charitable Trust Sequencing Centre, the MHTP High Content Screening Centre and the MHTP Microarray Centre.

The funding generously provided by the ACRF has allowed the expansion of the services provided by the MHTP, with the addition of next-generation sequencing capabilities.

This equipment allows the rapid sequencing of entire genomes, providing researchers with greater insights into the nature of the genes involved in cancer. Such insights are critical for the development of therapies to target individual cancers.

"THERE ARE NOW MORE THAN 300 STAFF AND STUDENTS CONDUCTING RESEARCH AT THE INSTITUTE, WHICH HAS DEVELOPED INTO A KEY PLAYER IN BIOMEDICAL RESEARCH."

DIRECTOR'S MESSAGE (CONTINUED)

I was pleased to host an MIMR Patrons Club event in August. The event highlighted research at MIMR over the past 20 years, as well as our vision for the future. The Patrons toured the four research centres, where they learnt about the latest advances in our research at MIMR. We are grateful to all our Patrons Club members for their ongoing interest and support of the Institute.

The annual Ron Evans Golf Day was a resounding success in raising funds for our bowel cancer research programs. More than 110 golfers took part in the event at the Royal Melbourne Golf Club, in honour of Ron Evans AM, who passed away from bowel cancer in 2007. My thanks go to the Evans Family for their continuing generous support of this special event.

2011 was a challenging year politically for Australia's medical research community. In March the Federal Government proposed cutting $400 million from the medical research budget, which would have had major negative consequences for our future research.

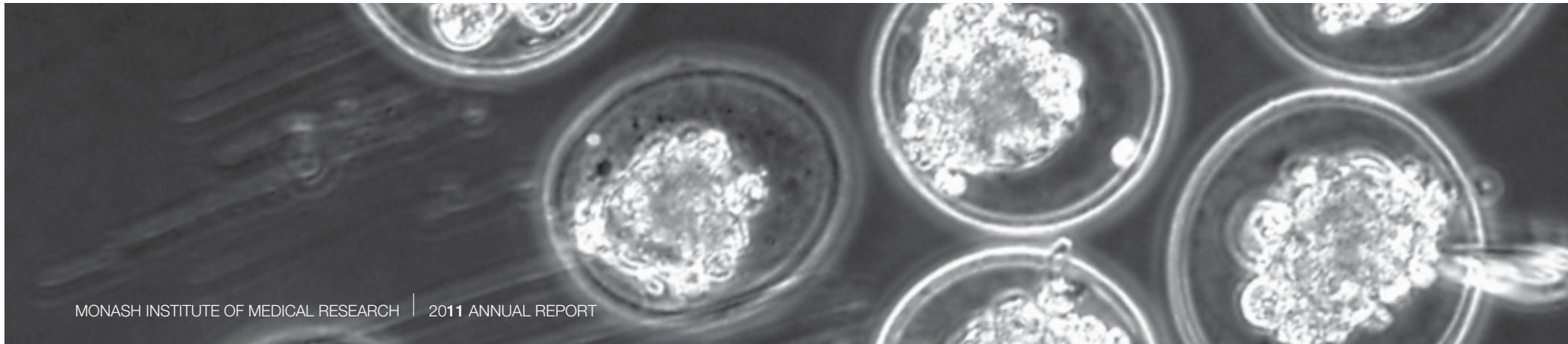
This proposal prompted the "Discoveries Need Dollars" campaign, with demonstrations and the lobbying of politicians by researchers and students throughout Australia. Thanks to the campaign, the cuts to medical research funding in the 2011-2012 Budget did not occur. However, it is essential that we remain vigilant to ensure that medical research remains a funding priority for the future.

This year, a number of MIMR researchers were awarded fellowships or funding for their research projects from the Federal Government, mainly through funding schemes administered by the National Health and Medical Research Council.

In addition, several researchers were successful in obtaining funding from a variety of philanthropic organisations. As always, we are grateful to the Federal and State Governments, and to our many philanthropic donors for their ongoing support of our research programs.

Professor Bryan Williams
Institute Director

CHAIRMAN'S MESSAGE



CHAIRMAN'S MESSAGE

It was a pleasure as Chairman of the Monash Institute of Medical Research to be able to witness the Institute's 20th Anniversary celebrations this year.

The Institute has come such a long way since its inception in 1991 as the Monash Institute of Reproduction and Development under Professors David de Kretser and Ian Trounsen, and the key research milestones it has unveiled along the way.

I look forward to seeing MIMR's future evolve and strengthen within the Monash Health Translation Precinct (MHTP) – a partnership between Southern Health, Prince Henry's Institute, Monash University and MIMR. In particular, I welcome the future launch of the new addition to the MHTP Genomics Facility, the ACRF Centre for Cancer Genomic Medicine for which we received $1.6 million in funding this year.

This year has seen the new Advisory Board establish itself. We farewelled Monash University's out-going Dean of Medicine, Nursing and Health Sciences Faculty Professor Steve Wesslingh and welcomed the new Dean, Professor Christina Mitchell.

Prof Mitchell joins the current board members Professors Ross Coppel, Paul Hertzog, Ian Smith, Bryan Williams, Adjunct Professor Adrian Walker, Ms Sue Williamson, Ms Barbara Crook, and Mr Robert Smorgon and myself.

The Director's Report covers the Institute's work over the past year, and does not require reiterating. However, I must take this opportunity to congratulate all researchers in achieving funding and research goals.

In particular I'd like to congratulate MIMR for achieving outstanding results in the Federal Government's new measurement of research excellence, the Excellence in Research for Australia Initiative (ERA).

Out of a possible score of 5, MIMR's ERA rating was 4.42 against the Group of 8 (GO8) universities, which averaged 3.98. A good 47 per cent of MIMR staff achieved an ERA rating of 5 and another 50 per cent had an ERA rating of 4. This new set of metrics is mostly based on journal publications and competitive grants.

> "OUT OF A POSSIBLE SCORE OF 5, MIMR'S ERA RATING WAS 4.42 AGAINST THE GROUP OF 8 (GO8) UNIVERSITIES, WHICH AVERAGED 3.98."

The research reputation of the University is largely supported by the FMNHS (Faculty of Medicine, Nursing & Health Sciences) with the ERA identifying three major areas of Monash as being well above world class, two of those in the medical area.

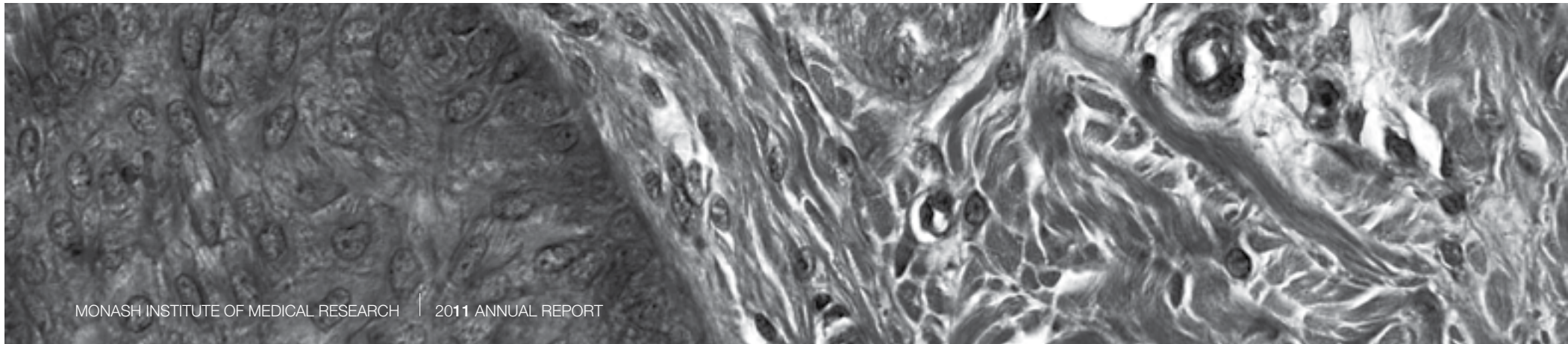
On behalf of all Board Members, thank you to Bryan, the Centre Directors, researchers, students and staff. To be successful in your research career, you require endless amounts of dedication, patience and enthusiasm. Your tireless work certainly does not go unnoticed. Thank you for all that you do.

Graeme Wise

Chairman
Monash Institute of Medical Research
Advisory Board

GOVERNANCE

MIMR Advisory Board



MIMR ADVISORY BOARD

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Chairman:
Adidem Group

Founder and Patron:
Big Issue street newspaper

Ms Barbara Crook

Chief Executive Officer:
Taxpayers Australia Inc and Superannuation Australia

Research Committee Member:
Taxpayers' Research Foundation Ltd

Board Member:
Monash University Medical Foundation

Board Member:
MIMR Foundation

Professor Ross Coppel

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

Professor Paul Hertzog

Deputy Director:
Monash institute of Medical Research

Director:
Centre for Innate Immunity and Inflammatory Diseases, Monash Institute of Medical Research

Professor Ian Smith

Pro-Vice Chancellor:
(Research and Research Infrastructure)
Monash University

Board Member:
Monash Centre for Synchrotron Science

Board Member:
Auspep Pty Ltd

Director:
Victorian Node, Proteomics Australia Consortium

Mr Robert Smorgon AM

Director:
Escor Group

Director:
Australian Council for Children and Youth Organisations

Adjunct Professor Adrian Walker

Trustee:
MIMR Foundation

Professor Steve Wesselingh

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

Professor Bryan Williams

Director:
Monash Institute of Medical Research

Director:
Centre for Cancer Research, Monash Institute of Medical Research

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Professor Christina Mitchell

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

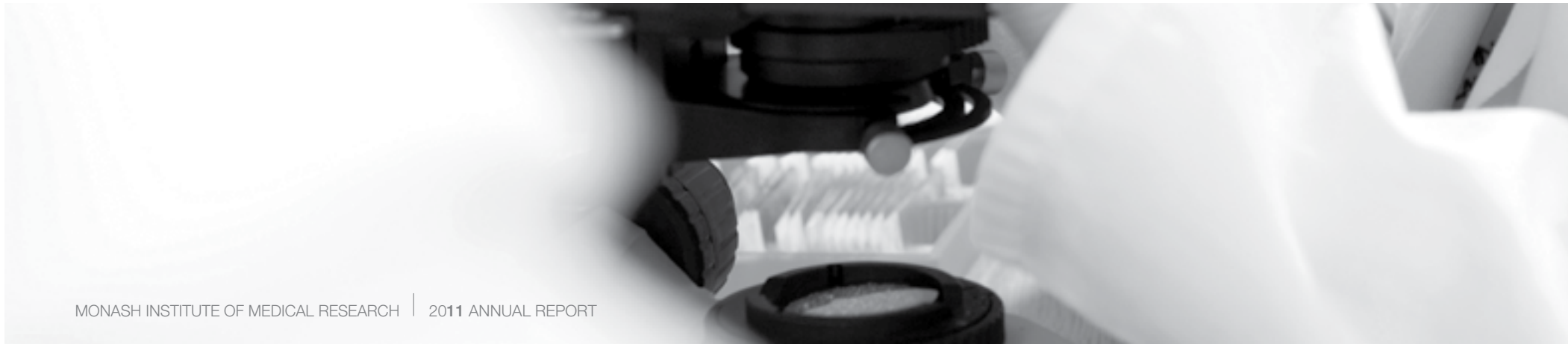
RESEARCH

Centre for Cancer Research

Centre for Innate Immunity and Infectious Diseases

Centre for Reproduction and Development

The Ritchie Centre



CENTRE FOR CANCER RESEARCH

Centre Director: Professor Bryan Williams

Research Group Leaders: Associate Professor Greg Hannigan, Associate Professor Terry Johns, Professor Neil Watkins, Dr Elizabeth Williams

Scientists in the Centre for Cancer Research conduct basic research into the molecular and cell signalling pathways underlying the development, growth and metastasis of tumours, and the links with innate immunity and inflammatory processes.

In addition, translational research into the development of novel anti-cancer therapeutics is carried out in the Centre, which also houses the Phase I Clinical Trials Program.

Several scientists in the Centre were awarded funding from the NHMRC for their research in 2011. Associate Professor Terry Johns received a project grant of $673,520 for his work on the development of new therapeutic strategies for the treatment of high grade glioma, and Dr Michael Gantier received a project grant of $483,660 for his work on the microRNA regulation of antiviral responses.

A CJ Martin Overseas Biomedical Fellowship was awarded to Dr Di Wu, who received $334,884 for her work on the analysis of interactions and mutation patterns among genes in human tissues using bioinformatics tools.

In addition, Dr Daniel Gough will relocate to the Centre from the New York University School of Medicine in 2012, on a Fellowship from the Leukemia & Lymphoma Society. He received project grant funding of $411,175 from the NHMRC for his research into the role of mitochondrial STAT3 in K-Ras-induced myeloid leukaemias.

Scientists in the Centre were also successful in their applications to other funding bodies in 2011. Dr Elizabeth Williams was awarded a New Directions Development Award of $300,000 by the Prostate Cancer Foundation of Australia for her work on castrate-resistant prostate cancer, and Drs Jason Cain, Michelle Van Sinderen and Jacqueline Donoghue were each awarded Early Career Seed Grants by the Victoria Cancer Agency.

Dr Cain, working with Professor Neil Watkins, received funding for his work on the development of a new biomarker of Hedgehog pathway activity in cancer, and Drs Van Sinderen and Donoghue, working with Associate Professor Terry Johns, both received grants for their research into novel therapies for the treatment of glioma.

Dr Donoghue was also awarded a grant from the Cure Cancer Australia Foundation for her research into agents to target proteins in glioma cells.

Dr Luciano Martelotto and Professor Neil Watkins received 2011 MIMR Flagship Project funding for their research into therapies to overcome acquired resistance to chemotherapy treatment in patients with small cell lung cancer. Using the High Content Screening Facility at MIMR, they carried out an extensive genetic screen to identify the cellular pathways that contribute to chemoresistance.

Together with their collaborators, including researchers from Stanford University and the Johns Hopkins University School of Medicine, USA, Dr Luciano and Professor Watkins co-authored a publication in the high-profile journal *Nature Medicine*.

CENTRE FOR CANCER RESEARCH (CONTINUED)

The paper, entitled "A crucial requirement for Hedgehog signaling in small cell lung cancer", generated a great deal of media interest. Dr Luciano also received the 2011 MIMR High Profile Publication Award for this paper (Park et al. 2011, *Nat Med* 17:1504-1508). A summary of the paper can be found in the Research Highlights section of this Annual Report.

Dr Afsar Ahmed joined the Centre in June 2011, as the 2011 Ron Evans Cancer Research Fellow. Dr Ahmed is investigating the role of integrin-linked kinase in bowel cancer, in collaboration with Associate Professor Greg Hannigan and Professor Bryan Williams.

Centre Director Professor Bryan Williams and Dr Ernest Borden (Cleveland Clinic, USA) were co-organisers and co-chairs of a symposium on Interferon Stimulated Genes and their Protein Products in 2011, which was held at the Monash University Prato Centre in Italy in October.

This satellite symposium was held after the 9th Joint Meeting of the International Cytokine Society (ICS) and International Society for Interferon and Cytokine Research (ISICR) in Florence, and was sponsored by ISICR, MIMR and the Cleveland Clinic.

Dr Michael Gantier, Dr Anthony Sadler and Dr Aaron Irving were each awarded 2011 Milstein Travel Awards by ISICR to attend the ISICR/ICS joint meeting in Italy. Dr Gantier was also awarded a prize for the best gene therapy paper by the Australasian Gene Therapy Society for his research article in *Nucleic Acids Research* entitled "Analysis of microRNA turnover in mammalian cells following Dicer1 ablation" (Gantier et al. 2011, *Nucleic Acids Res* 39:5692–5703). A summary of the findings of this well-cited paper is provided in the Research Highlights section.

In 2011, the Phase I Clinical Trials Program commenced a "first-time-in-human" study of a new drug that targets abnormal cell division in cancers by inhibiting aurora kinase oncoproteins. Other early-phase trials open at MIMR and Monash Medical Centre are investigating agents that target cancer stem cells.

These include studies of novel Hedgehog pathway inhibitors in patients with advanced small cell lung cancer or chondrosarcoma, and a Notch pathway inhibitor in non-small cell lung cancer. In addition, analysis of completed Phase I studies of vascular-targeted agents in advanced solid tumours and glioblastoma was commenced.

Research Highlights

A crucial requirement for Hedgehog signaling in small cell lung cancer

Lung cancer is the most common cause of cancer death in Australia and about 15-20 per cent of cases are SCLC, a highly aggressive form of the disease. SCLC is very sensitive to chemotherapy, but rarely cured because the tumour grows back. Tumour regrowth following complete remission is not well understood as it is difficult to identify small populations of residual tumour cells.

Signalling pathways maintaining normal stem cells are quite different from those that drive growth. One of these pathways, known as "Hedgehog" has been identified as being very important in normal stem cells, and in some cancers.

Unlike conventional cancer therapies, Hedgehog inhibitors are not effective in most established tumours. Instead, they appear to work by blocking the ability of cancers to regenerate from a small residual number of cells.

Several pharmaceutical companies have developed a new generation of Hedgehog inhibitors that are now in early phase clinical trials. Based on Prof Watkin's study, these drugs will not be effective in advanced SCLC, but they may be effective in blocking regeneration of cancers like SCLC following chemotherapy.

Park KS, Martelotto LG, Peifer M, Sos ML, Karnezis AN, Mahjoub MR, Bernard K, Conklin JF, Szczepny A, Yuan J, Guo R, Ospina B, Falzon J, Bennett S, Brown TJ, Markovic A, Devereux WL, Ocasio CA, Chen JK, Stearns T, Thomas RK, Dorsch M, Buonamici S, Watkins DN, Peacock CD, Sage J (2011) A crucial requirement for Hedgehog signaling in small cell lung cancer. *Nat Med* 17:1504-1508.

CENTRE FOR CANCER RESEARCH (CONTINUED)

Activation of Src induces mitochondrial localisation of de2-7EGFR (EGFRvIII) in glioma cells: implications for glucose metabolism

The epidermal growth factor receptor (EGFR) is a protein that has a critical role in the development of normal cells. In glioma, the most lethal of the brain cancers, the EGFR is altered. These alterations result in uncontrolled activation of the EGFR, causing signals that promote the growth and survival of brain cancer.

Mitochondria are the powerhouses inside the cell that provide the energy for growth. In this paper we show that when glioma cells are stimulated to grow this altered EGFR moves from the cell surface to the mitochondria.

The altered EGFR enhances mitochondria function allowing it to produce the energy required for cell division. These studies suggest that blocking the altered EGFR from moving to the mitochondria might help prevent the growth of glioma clinically.

Cvrljevic AN, Akhavan D, Wu M, Martinello P, Furnari FB, Johnston AJ, Guo D, Pike L, Cavenee WK, Scott AM, Mischel PS, Hoogenraad NJ, Johns TG (2011) Activation of Src induces mitochondrial localisation of de2-7EGFR (EGFRvIII) in glioma cells: implications for glucose metabolism. *J Cell Sci* 124:2938-2950.

Analysis of microRNA turnover in mammalian cells following Dicer1 ablation

MicroRNAs are small molecules recently discovered which critically regulate gene expression. MicroRNAs are deregulated in cancers, and because they can easily be detected in the blood, they present novel opportunities for the early detection of cancer .

In this work, we were interested in defining how stable are miRNAs following synthesis by the cell. Our results established that microRNAs are very stable which was important to know the time frame where miRNAs can be used as markers in cancer detection.

Gantier MP, McCoy CE, Rusinova I, Saulep D, Wang D, Xu D, Irving AT, Behlke MA, Hertzog PJ, Mackay F, Williams BRG (2011) Analysis of microRNA turnover in mammalian cells following Dicer1 ablation. *Nucleic Acids Res* 39:5692–5703.

CENTRE FOR INNATE IMMUNITY AND INFECTIOUS DISEASES

Centre Director: Professor Paul Hertzog

Senior Scientists: Associate Professor Richard Ferrero, Associate Professor Brendan Jenkins, Dr Ashley Mansell, Dr Carl Sprung, Professor Phil Bardin

The Centre for Innate Immunity and Infectious Diseases researches the molecular regulation of the innate immune response. This early immune response determines how the body responds to infection by pathogens.

The Centre for Innate Immunity and Infectious Diseases researches the molecular regulation of the innate immune response. This early immune response determines how the body responds to infection by pathogens. It initiates the inflammatory response and can modulate the development of some cancers.

By understanding the molecular pathways that regulate these processes as well as their normal, physiological roles, researchers working in the Centre aim to contribute to developing new approaches for the prevention, diagnosis and treatment of disease.

The research undertaken within the Centre requires considerable funding to support salaries, student scholarships, consumables and equipment. The funding is obtained through hard work of the researchers, for whom a significant part of their time is devoted to preparing grant applications. In a climate of tough government Budget constraints where less than 25 percent of applications are funded, 2011 was an outstanding year for the Centre, with 58 percent of applications to the National Health and Medical Research Council (NHMRC) and Australian Research Council (ARC) successful. This will underpin the Centre's research efforts for the next three years.

The Molecular Immunity Laboratory, led by Professor Paul Hertzog, was awarded three grants from NHMRC and ARC to support their investigations into the role of a novel cytokine in regulating immune responses in the female reproductive tract.

This is exciting new research into reproductive tract infections such as HIV, HPV, HSV and Chlamydia which represent major health and socioeconomic problems worldwide. This funding includes the award of a prestigious five-year ARC fellowship to Dr Niamh Mangan who came to the Centre from Trinity College, Dublin, to work on this problem.

The Gastrointestinal Infection and Inflammation Laboratory, led by Associate Professor Richard Ferrero, was awarded two grants from the NHMRC, as well as an ARC Discovery grant which was awarded to Dr Maria Kaparakis-Liaskos. These grants will support investigations into the disease-associated roles of Helicobacter pylori, a bacterium that infects half of the global population and is the major cause of stomach cancer and peptic ulcer disease.

In addition to these research programs, Dr Cody Allison was awarded a one-year Fellowship from the Cancer Council Victoria to pursue work on a potential new link between a known inflammatory molecule and the development of gastric cancer.

CENTRE FOR INNATE IMMUNITY AND INFECTIOUS DISEASES (CONTINUED)

The Cytokine Signalling Laboratory, led by Associate Professor Brendan Jenkins, has been awarded multiple grants from the NHMRC, Cancer Council of Victoria and the Association for International Cancer Research to support their investigations into the role of cytokines in promoting cancer of the lung and stomach, the two most common causes of cancer-related deaths worldwide.

Dr Ashley Mansell's Toll-like Receptor (TLR) Signalling Laboratory received two NHMRC grants to further their research into the role of the TLR signalling pathways in human innate immunity. These diverse projects will provide a structural analysis of key signalling molecules involved in generating the inflammatory response to infections, thus providing potential therapeutic treatments.

In conjunction with Associate Professor Mark Hedger, the laboratory will also investigate the role of Toll-like receptors in male reproduction and sperm development. These studies further highlight the pervasive role of innate immunity in multiple facets of human health.

The DNA Repair & Genomics Laboratory, led by Dr Carl Sprung, has been awarded grants from the NHMRC, NIH and DoHA/ Cancer Australia to support research to improve cancer treatment.

Investigation of the molecular mechanisms underlying the responses to DNA damage caused by radiation such as that received during cancer radiotherapy and the development of novel radiotherapy strategies, including those which make use of the local Australian Synchrotron, are major areas of interest.

The Respiratory Infection and Inflammation Laboratory, headed by Professor Phil Bardin, investigate the role of virus infections (rhinovirus and respiratory syncytial virus) in lung diseases.

Recent research by Drs Belinda Thomas and Michelle Tate has demonstrated deficient immune responses in asthma. This has been found to be linked to a key pro-inflammatory and pro-fibrotic molecule.

Other studies have examined nuclear trafficking of rhinovirus proteins, conducted in collaboration with Professor David Jans and Dr Reena Ghildyal at Monash University. The research is funded by collaborative NHMRC, Asthma Victoria and Lung & Sleep Medicine grants.

Research highlights

The molecular pathogenesis of STAT3-driven gastric tumourigenesis in mice is independent of IL-17

Stomach inflammation (gastritis) is strongly associated with Helicobacter pylori bacterial infection, and can also progress to gastric cancer.

However, it remains largely unknown how Helicobacter triggers these gastric diseases in people. Using a mouse model, which develops gastric inflammation and tumours, our aim was to determine the role of the IL-17 protein in stomach cancer since this protein is a potent pro-inflammatory agent.

Our work showed that while IL-17 production appeared to be important for gastric inflammation, it did not contribute to gastric cancer.

Kennedy, C.L., Najdovska, M., Jones, G.W., McLeod, L., Hughes, N.R., Allison, C., Ooi, C.H., Tan, P., Ferrero, R.L, Jones, S.A., Dev, A., Sievert, W., Bhathal, P.S., Jenkins, B.J. (2011) The molecular pathogenesis of STAT3-driven gastric tumourigenesis in mice is independent of IL-17. J. *Pathology.* 225:225-264

Suppressor of cytokine signalling (SOCS)1 inhibits type I interferon (IFN) signalling vial the IFNAR1 associated tyrosine kinase

Interferons (IFN) are crucial proteins that play multiple roles in maintaining health and well-being, while also playing an important role in fighting infection through the anti-viral immune response. Having such crucial functions, it is critically important to regulate the expression and responses of IFNs. If not controlled correctly, IFNs can cause chronic disease or even death.

This publication characterises the molecular mechanism of how IFN signalling is regulated by the key suppressor of cytokine signalling, SOCS1, for the generation of an appropriate immune response to viral and bacterial infections.

This study establishes for the first time that SOCS1 does not directly bind the IFN receptor to control signalling, but rather interacts with a protein called Tyk2 that is recruited to the receptor to initiate downstream signalling. This interaction also regulates the activation status of Tyk2.

CENTRE FOR INNATE IMMUNITY AND INFECTIOUS DISEASES (CONTINUED)

This study provides an insight as to how IFN responses are manipulated, and thus may contribute to better treatments of IFN-mediated diseases or to enhancing the therapeutic effects of IFN in treating such diseases as multiple sclerosis or viral hepatitis.

Piganis, R., De Weerd, N., Gould, J., Schindler, C., Mansell, A., Nicholson, S., Hertzog, P., (2011) Suppressor of cytokine signalling (SOCS)1 inhibits type I interferon (IFN) signalling vial the IFNAR1 associated tyrosine kinase, Tyk2, *J.Biol Chem*, 286, (39): 33811-33818

Alternative transcript initiation and splicing as a response to DNA damage

Ionizing radiation is a major DNA damaging agent that can be produced by both natural and man-made sources. Humans are exposed to ionizing radiation from background radiation, medical treatments, occupational and accidental exposures. Ionizing radiation can affect many biological processes.

One such critical process is the conversion of genes to RNA, called transcription. Alternative transcription is part of this process, but little is known about this aspect in response to ionizing radiation on a genome-wide basis.

We have examined this in human cells using exon microarrays to comprehensively characterize radiation-induced transcription expression products. This paper provides the first genome-wide view of the transcriptional response to ionizing radiation at the exon level.

Previously uncharacterized alternative transcripts induced following ionizing radiation exposure have been discovered. Of particular interest was the discovery of alternative transcription initiation in response to ionizing radiation for a relatively large number of ionizing radiation responsive genes.

Also, clusters of co-ordinately up- and down-regulated radiation response genes were identified at specific chromosomal loci.

This study provides novel insights into alternative transcripts as a mechanism for response to DNA damage and cell stress responses in general. Understanding the molecular response to radiation is essential since it is used regularly in medicine (e.g. radiotherapy and X-ray imaging), but is also able to cause cancer.

The resulting understanding of basic radiobiological responses will ultimately result in new therapeutics, for example, in conjunction with radiotherapy cancer treatment.

Sprung, C.N., Li, J., Hovan, D., McKay, M.J., Forrester, H.B. *Alternative transcript initiation and splicing as a response to DNA damage, PLoS One.* 2011:6(10):e25758. Epub 2011, October 19.

CENTRE FOR REPRODUCTION AND DEVELOPMENT

Centre Director: Professor Justin St John

Senior Scientists: Professor David de Kretser, Associate Professor Mark Hedger, Dr Ursula Manuelpillai, Dr Paul Verma, Dr Patrick Western

The Centre for Reproduction and Development conducts research into how human disease is propagated and transmitted using innovative reproductive, developmental and stem cell biology approaches.

The Centre for Reproduction and Development conducts research into how human disease is propagated and transmitted using innovative reproductive, developmental and stem cell biology approaches.

Since taking up the position of Centre Director in late 2009, Professor Justin St John has made significant progress toward refocusing the research of the Centre to converge on furthering the understanding of specific processes underlying genetic and epigenetic basis of disease.

Critical research that was carried out by CRD scientists in 2011 involved investigating how amnion cells can be used for transplantation purposes and how somatic cells can be reprogrammed to behave as stem cells.

Dr Ursula Manuelpillai has been actively engaged with her prestigious Monash University's Monash Research Accelerator Award to help fast-track her career. This enables her to promote her amnion stem cell work in the translational research environment modeling and repairing liver fibrosis.

Dr Paul Verma has continued to work on producing induced pluripotent stem cells; cells from a part of the body such as skin that are reprogrammed to act as embryonic stem cells.

Prof St John continues to use stem cells to understand mitochondrial DNA replication and transmission.

The Centre's work in mitochondrial disease has expanded further into mitochondrial protein biochemistry with the appointment this year of Dr Matthew McKenzie from La Trobe University.

Research in the field of germ cell development by Dr Patrick Western is also being developed to look at how genetic and epigenetic processes during early germ cell development can give rise to germ cell tumours and effect patterns of inheritance than can lead to a range of diseases.

Our work in tumour cell biology has been further expanded into genomic and epigenetic analysis with the appointment this year of Dr Stefan White from the Murdoch Children's Research Institute

In 2011, we also celebrated the return of our founder, Emeritus Professor David de Kretser AC, following a five-year sabbatical as Governor of Victoria, who with Associate Professor Mark Hedger, is continuing the Centre's renowned work into the role of the hormone follistatin in reproductive biology and transplantation, and the variety of roles that come with having a such a well-respected international reputation in this field.

A/Prof Hedger successfully had his NHMRC Research Fellowship renewed. Prof St John was also awarded an NHMRC project grant to develop stem cell models of mitochondrial DNA disease.

CENTRE FOR REPRODUCTION AND DEVELOPMENT (CONTINUED)

Research highlights

Generation of stable pluripotent stem cells from NOD mouse tail-tip fibroblasts

Type 1 diabetes (T1D or Diabetes mellitus type 1, formerly known as insulin dependent or juvenile diabetes) is a serious, life-long condition, which causes major health, social and economic burden for individuals with the disease, their families and the community.

Australia remains among the top 10 countries with the highest rates of T1D in children. Incidence varies from 19 to 24 per 100,000 for the last 10 years in Australia. There were over 8,000 new cases of T1D diagnosed in Australian children between 2000 and 2008, an average of two new cases every day as per the Australian Institute of Health and Welfare*.

T1D is a polygenic disease, meaning multiple genes contribute to its onset. Non-obese diabetic (NOD) mice spontaneously develop T1D in a manner similar to humans with more than 50 of the genes associated with T1D shared between mice and humans. Therefore, NOD mice provide an invaluable model for investigating T1D pathogenesis under controlled genetic and environmental conditions in the laboratory.

In the present article, we generated the induced pluripotent stem cells (iPSC), a substitute for embryonic stem cells, from adult NOD mouse cells.

Though repeated injection of insulin is the most common method for T1D treatment, other long-term alternatives such as stem cells-based cell transplantation are being investigated. The iPSC lines generated in this study provide a novel source of cells to elucidate T1D pathogenesis as well as treatments via cell transplantation.

**AIHW 2010. Incidence of T1D in Australian children 2000-2008. Diabetes series no. 13. Cat. no. CVD 51. Canberra: AIHW.*

Liu J, Ashton MP, Sumer H, O'Bryan MK, Brodnicki TC, Verma PJ (2011) Generation of stable pluripotent stem cells from NOD mouse tail-tip fibroblasts. *Diabetes* 60(5):1393-8.

Mutations in the gene encoding C8orf38 block complex I assembly by inhibiting production of the mitochondria-encoded subunit ND1

Mitochondria are the 'powerhouses' of the cell, oxidizing fats and sugars to generate ATP, a molecule used as an energy unit to drive many cell functions.

Disruption of this process can result in mitochondrial disease, affecting approximately 1 in 5,000 live births. In most cases these disorders are untreatable and therefore prognosis remains poor for affected patients. Of these disorders, defects in Complex I of the mitochondrial respiratory chain are the most common.

This large complex is comprised of 45 different protein subunits, and in the last 6 years proteins which aid its assembly ('assembly factors') have also been identified. However, how these assembly factors function remains largely unknown.

In this manuscript we have characterised human C8orf38, an assembly factor of Complex I. Using skin cells from a patient with mitochondrial disease, we showed that loss of C8orf38 leads to severe depletion of complex I due to defects in specific structural subunits. We were also able to detect new complexes which represent different assembly stages of complex I in these patient cells, allowing us to refine the current model for complex I assembly.

McKenzie M, Tucker EJ, Compton AG, Lazarou M, George C, Thorburn DR, Ryan MT (2011) Mutations in the gene encoding C8orf38 block complex I assembly by inhibiting production of the mitochondria-encoded subunit ND1. *J Mol Biol* 414(3):413-26.

Identification of SOX3 as an XX male sex reversal gene in mice and humans

Our gender is determined by our DNA. In males, testis development occurs in the presence of the *SRY* gene on the Y chromosome. When *SRY* is not present, ovarian development in females occurs.

Disorders of sex development (DSD) are the result of a disruption in testis or ovary development. One class of DSD is testicular development in the absence of *SRY*. Using whole genome microarrays, we showed that a significant proportion of such DSD cases are due to DNA rearrangements around the *SOX3* gene. *SOX3* is a close relative of *SRY*, and is normally expressed in the brain.

We hypothesized that the similarity between *SRY* and *SOX3* meant that *SOX3* could functionally replace *SRY*, if expressed in the appropriate tissue at the right time. Indeed, *in vivo* studies showed that *SOX3* expression, in the developing gonad, was sufficient to drive testis development in the absence of *SRY*. Additionally, *in vitro* studies showed that *SOX3* could substitute for *SRY* in driving the expression of testis-development genes.

This finding will aid in the diagnosis of DSD, and provides an example of how mutations affecting expression of a specific gene can lead to a developmental disorder, even when that gene is not normally expressed in the affected tissue.

Sutton E, Hughes J, White S, Sekido R, Tan J, Arboleda V, Rogers N, Knower K, Rowley L, Eyre H, Rizzoti K, McAninch D, Goncalves J, Slee J, Turbitt E, Bruno D, Bengtsson H, Harley V, Vilain E, Sinclair A, Lovell-Badge R, Thomas P (2011) Identification of SOX3 as an XX male sex reversal gene in mice and humans. *J Clin Invest* 121(1):328-41.

THE RITCHIE CENTRE

Centre Director: Professor Euan Wallace

Deputy Directors: Dr Caroline Gargett, Professor Stuart Hooper, Associate Professor Rosemary Horne, and Professor Graham Jenkin

Research Group Heads: Professor Stuart Hooper, Associate Professor Rosemary Horne, Professor Graham Jenkin, Dr Caroline Gargett, Associate Professor David Walker

The Ritchie Centre fulfills the role of the principal research centre of the Monash University Department of Obstetrics and Gynaecology, incorporating the Centre for Women's Health Research, and is a major research partner of the Department of Paediatrics at the Southern Clinical School.

Its mission is to improve the health of women, infants and children through innovative research that informs better healthcare.

In 2011, The Ritchie Centre consolidated on the significant expansion that took place at the beginning of 2010 under the incoming Director of Professor Euan Wallace. The Centre now has over 150 research staff and students; including fetal physiologists, sleep physiologists, immunologists, stem cell biologists, neonatologists, paediatricians, obstetricians, gynaecologists, and radiologists.

It has translational research partnerships with Victoria's largest health service, Southern Health, through Monash Women's Hospital, Monash Children's Hospital, Monash Newborn, and The Melbourne Children's Sleep Centre. The Ritchie Centre offers a unique setting where research developments can be rapidly applied for the benefit of women, seriously ill infants and children. This has lead to rapid translation of its basic research into clinical trials and clinical practice.

Securing funding for their research continues to play a major role in the activities of the Centre's scientists. In 2011, funding success included government, philanthropic and industry grants. Ritchie researchers were successful in securing NHMRC funding including four new NHMRC Project Grants, a Career Development Fellowship to Dr Graeme Polglase, a Neil Hamilton Fairley Clinical Fellowship to Dr Ryan Hodges, a Principal Research Fellowship to Associate Professor David Walker and a Health Professional Early Career Fellowship to Dr Flora Wong. Dr Polglase was awarded the inaugural Al and Val Rosenstrauss Medical Research Fellowship from The Rebecca L. Cooper Medical Research Foundation.

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) also awarded Research Foundation Scholarships and Fellowships to four Centre recipients. In addition, 2011 saw awards from the Society for Reproductive Biology and the American Foundation for Endometriosis to Dr Caroline Gargett—both for Research Excellence in Women's Health, awards to the husband and wife research team Drs Marcel and Claudia Nold, who received the Georges Koehler award and Claudia the Christina Fleischmann Memorial Award for Young Women Investigators, respectively, and the Monash University Mollie Holman Doctoral Medal was awarded to Dr Scott Sands for the best PhD thesis in the Faculty of Medicine, Nursing and Health Sciences.

THE RITCHIE CENTRE (CONTINUED)

Further Government funding included grants from the Australian Stem Cell Centre, the CSIRO and the Education Investment Fund for Translating Health Discovery. The latter being a $2 million grant for facilities to develop clinical translation of cell-based therapies. Significant Industry funding continues to be provided by the Australian based adult stem cell company, Mesoblast Australia, for preclinical and clinical trials directed at repair and replacement of damaged and diseased spinal discs.

Philanthropic funding included a Grand Challenges Explorations Grant from the Bill and Melinda Gates Foundation for Innovative Global Health Research to trial the use of melatonin as a potential treatment for neonatal brain injury.

Funding was also secured from the Matsarol Foundation to support research staff and to upgrade equipment for advancing research into brain injury in newborn babies and the application of stem cells to improve health outcomes for babies and adults; the Cerebral Palsy Alliance AVANT Innovative Research Grant fund to further research into preventing brain injury in premature babies; the Walter Cottman Endowment Fund to investigate a cell-based therapy for the treatment of pelvic organ prolapse; the Arthur and Mary Osborne Charitable Trust to investigate how stress and illness in pregnancy affects behavioural outcomes in the next generation; the Australian Cystic Fibrosis Research Trust to investigate the use of amnion stem cells for the treatment of cystic fibrosis. The Asthma Foundation of Victoria (Helen Macpherson Smith Trust) and the Jack Brockoff Foundation supported our research into broncho-pulmonary disorder in premature babies and The Scottish Cot Death Trust and Foundation for the Study of Infant Deaths (UK) provided funding for research into the mechanisms of the Sudden Infant Death Syndrome, while The Research Foundation of the Cerebral Palsy Alliance provided funds to support research into brain injury in premature babies.

Blair Ritchie's bequest continues to allow us to support young scientists, purchase essential equipment and run innovative experiments, which we otherwise would not be able to support. It is only through the generosity of individuals and philanthropic donors that the Centre can develop and grow as Government funding can never support an entire research project.

The Ritchie Centre's annual Colloquium *"Cell Therapies & Regenerative Medicine"*, was held in late 2011 and included a public forum at the BMW Edge Theatre at Federation Square, entitled *"Cerebral Palsy – Treatments for Tomorrow"*. The forum featured a strong panel of international specialists, including Professor Nadia Badawi, Associate Professor Paolo de Coppi, Professor Charles Cox, Professor Alan Trounson and Centre Scientists Drs Suzie Miller and Graeme Polglase.

More than 150 members of the public attended the session, which highlighted recent technical research developments and provided the opportunity for the panel to inform the public about progress being made to prevent and treat cerebral palsy.

The Ritchie Centre's annual Kaarene Fitzgerald Public Lecture this year was titled "What's new in SIDS research and safe sleeping recommendations in 2011". Invited speakers were Dr Dawn Elder from the University of Otago, New Zealand and Dr Jhodie Duncan from the Florey Neuroscience Institutes, Melbourne. The Centre's own Associate Professor Rosemary Horne also spoke. Over 150 nurses, midwives, SIDS councilors and parents attended.

New recruits in 2011 included the appointment of Dr Ilias Nitsos as the Manager of our expanding experimental surgical facilities; but the Centre lost one of its key administrators when Jill McFadyean left the Centre and University after many years of loyal service.

Jill was originally employed by Professor Alan Trounson to the Centre for Early Human Development at the Monash Institute of Reproduction and Development, before it changed its name to MIMR. She subsequently held many administrative roles in the University before returning to The Ritchie Center with Graham Jenkin in 2010. We thank Jill for her dedicated service to MIMR and the Centre. She was replaced by Dr Yen Pham in 2011.

Research Highlights

Improved breathing support may help preterm babies avoid brain damage

The Ritchie Centre's Dr Graeme Polglase's paper exploring ventilation injuries in preterm babies has been published in one of the most prestigious international publications, the United States' Journal of Applied Physiology. This journal has one of the highest impact factors in Neonatology.

Dr Polglase's paper, "Inflammation *in utero* exacerbates ventilation-induced brain injury in preterm lambs", paves the way for improving respiratory support to preterm babies and babies that have suffered from inflammation while in the womb.

Each year in Australia, around eight per cent of babies (around 24,000) are preterm and those less than 28 weeks old often suffer from respiratory or brain injuries, as well as an increased risk of cerebral palsy and neurodevelopmental problems. Inflammation in the womb is one of the major causes of preterm births.

This inflammation is often caused by bacterial infections moving from the vagina into the amniotic sac and ultimately infecting the fetus. Often when preterm babies are delivered they are sick or inflamed, and while clinicians treat and resuscitate them there is currently only one standard way of resuscitating babies. This standard resuscitation is not well-monitored.

THE RITCHIE CENTRE (CONTINUED)

As a result, this treatment can cause injury and therefore heightens the risk of brain haemorrhage and white matter damage, which leads to long-term adverse neurodevelopment and cerebral palsy. Dr Polglase is currently looking at improvements that can be made to initial care for preterm infants to improve the detrimental impacts on brain injuries and multi-organ damage.

This paper looks at the potential effects caused by unsafe ventilation support, which essentially, could increase the risk of lung and brain injury. It demonstrates that the initiation of ventilation in preterm neonates results in brain injury through two major pathways: 1) pulmonary, cardiovascular and subsequently cerebral haemodynamic instability and 2) the initiation of a pulmonary inflammatory response, which enters the systemic circulation, resulting in brain inflammation.

This paper also demonstrated that intrauterine inflammation prior to ventilation results in increased brain inflammation and injury. Inflammation *in utero* is a common in preterm infants, and is known to increase the incidence and severity of brain injury and long term morbidities including cerebral palsy. Importantly, this paper identifies a potential critical window for therapy to reduce the severity of brain injury in preterm neonates.

Polglase G.R., Nitsos I., Baburamani A.A., Crossley K.C., Slater M.K., Gill A.W., Allison B.J., Moss T.J.M., Pillow J.J., Hooper S.B. and Kluckow M. Inflammation in utero exacerbates ventilation induced brain injury in preterm lambs. *J Appl Physiol.* 2012;112(3):481-9.. Impact Factor: 3.75.

New model to study the development of the human female reproductive tract

The Ritchie Centre's PhD student Louie Ye's publication describing a protocol he developed to study human female reproductive tract development using human embryonic stem cells was published in the world's largest scientific journal, PLOS ONE. This highly respected open access, on line, peer-reviewed journal published >13,700 articles in 2011, covering all disciplines in science and medicine.

Mr Ye's paper, "Generation of human female reproductive tract epithelium from human embryonic stem cells" provides a tractable model for examining early developmental events in the human female reproductive tract.

The human female reproductive tract develops in the fetus around 22 weeks gestation from an invagination of the coelomic epithelium, which originally arises during embryo development. This invagination then develops into the Müllerian Duct, a precursor tube-shaped organ which subsequently develops into the Fallopian tubes, uterus and upper vagina.

These processes have previously been studied in mice, but until this publication there was no model for examining human female reproductive tract development. This new model can be applied to examine how exposure of the female fetus to endocrine disruptors and other chemicals during pregnancy may lead to reproductive tract cancers many years later in young women.

The model developed by Mr Ye involves a 2 step procedure to recapitulate the developmental stages of the female reproductive tract. The first step is conducted in vitro and involves inducing fluorescent-labeled human embryonic stem cells to differentiate into mesoderm by several growth factors (BMP4, Activin A) during embryoid body formation. Subsequently individual embryoid bodies are individually recombined with inductive neonatal mouse uterine mesenchyme to produce a recombinant tissue.

This induces further differentiation into intermediate mesoderm, the precursor of the Müllerian Duct. In the second step, the recombinant tissues are transplanted into immunocompromised mice for up to 8 weeks to allow further differentiation into mature tissues in vivo.

During this time, the recombined tissues differentiated first into Müllerian Duct-like cells expressing characteristic transcription factors, LIM1 and HOXA10, and then into mature ciliated reproductive tract epithelium, which expressed estrogen receptors. The reproductive tract epithelium was functional and proliferated in response to administered estrogen and secreted estrogen-dependent molecules.

It is possible that in the future, this new strategy could also be applied to patient specific induced pluripotent cells (iPS cells) in place of human embryonic stem cells. Such iPS cells may eventually have clinical application for women with Asherman's syndrome, who lack a functional endometrium, or women with intra-uterine adhesions, to regenerate their endometrium in vivo.

Ye L, Mayberry R, Lo C, Britt K, Stanley EG, Elefanty AG, Gargett CE (2011) Generation of human female reproductive tract epithelium from human embryonic stem cells. *PLOS ONE* 6(6) e21136. IF 4.411.

EDUCATION

Visiting Speakers 2011

MIMR Postgraduate Committee

Community Education and Education Events

Andrology Australia

2011 Graduates

VISITING SPEAKERS

Professor Linda Penn

Ontario Cancer Institute, University of Toronto

Targeting metabolism and the mevalonate pathway to trigger tumor cell death

14/02/11

Professor Paula Pitha

John Hopkins University

IRF-5 linking innate immune response to auroimmune disease and cancer

14/02/2011

Dr Jamie Wilson

Chief Editor, Nature Immunology

How to publish in Nature Immunology

21/02/2011

Professor Eicke Latz

Department of Infectious Diseases and Immunology, University of Massachusetts & Director of the Institute of Innate Immunity, University of Bonn

Role of the inflammasome in inflammation

22/02/2011

Professor Sean Grimmond

Director of the Queensland Centre for Medical Genomics, at the Institute of Molecular Biology, University of Queensland

Defining the molecular landscape of cancer genomes

17/03/2011

Professor Lois Salamonsen

Prince Henry's Institute

Endometrial receptivity: a critical step in establishing pregnancy

24/03/2011

Professor Eva Simpson

Prince Henry's Institute

Obesity, aromatase and breast cancer - old wine in new bottles

31/03/2011

Associate Professor Ian Trounce

Glaucoma Research Unit, Centre for Eye Research Australia

The less you eat the more you see: Rejuvenating mitochondria in the aging optic nerve

06/04/2011

Professor David Vaux

Walter and Eliza Hall Institute of Medical Research

Ten rules for the presentation and interpretation of data in publications

07/04/2011

Professor Andreas Meinhardt

Department of Anatomy and Cell Biology, Justus-Liebig-University Giessen, Germany

Evading the testicular immune response – pathogenic causes of male infertility

(14/04/2011)

Professor Murray Mitchell

Director University of Queensland Centre for Clinical Research

Epigenetics and the next generation

21/04/2011

Professor Neil Watkins

Monash Institute of Medical Research

Hedgehog Signalling: from files to clinical trials

05/05/2011

Professor Ken Korach

National Institute of Environmental Health Sciences – NIH, North Carolina, USA

New mouse models for dissecting estrogen receptor activities

11/05/2011

Professor John McNeil

School of Public Health and Preventative Medicine

ASPREE and the epidemiology of aging

12/05/2011

Professor Stephen M. Jane

Head, Central Clinical School, Monash University Director of Research, The Alfred Faculty of Medicine, Nursing and Health Sciences

Translational research - from the mouse to the bedside

19/05/2011

Professor Alberto Avolio

Australian School of Advanced Medicine, Macquarie University

Cellular and molecular mechanisms of arterial stiffness

26/05/2011

Professor Louise Hull

The Robinson Institute, University of Adelaide

Epigenetics in Endometriosis: the role of microRNAs

02/06/2011

VISITING SPEAKERS (CONTINUED)

Dr Bernd Timmerman

Next Generation Sequencing Core Facility, Max Planck Institute for Molecular Genetics, Berlin

The Use of Next Generation Sequencing and Sequence Capture to Study Human Genome Variation and Cancer

07/06/2011

Associate Professor Greg Hanigan

Monash Institute of Medical Research

From adhesion plaques to primary cilia: Integrin-Linked Kinase is a Hedgehog-Linked Kinase

09/06/2011

Dr Kelly Ewen-White

Life Technologies

Ion Torrent Sequencing Seminar

14/06/2011

Professor James Friend

Department of Mechanical and Aerospace Engineering, Monash University; Co-Director, MicroNanophysics Research Laboratory

Applications of High-Frequency Ultrasonics in Microfluidics and Microactuation

16/06/2011

Professor Wolfgang Weninger

Professor and Head Immune Imaging Program, Centenary Institute for Cancer Medicine and Cell Biology, University of Sydney

Visualising immune responses in real time

07/07/2011

Associate Professor Elizabeth Woodcock

Baker IDI Heart and Diabetes Institute

Identification of targets for treatment of hypertrophy and heart failure

14/07/2011

Associate Professor Roslyn Boyd

Queensland Cerebral Palsy and Rehabilitation Research Centre, Univesity of Queensland Department of Paediatrics

Can training change the brain: neuroscience outcomes of an RCT of constraint induced movement therapy vs bimanual training in congenital hemiplegia

28/07/2011

Associate Professor Claire Scott

Walter and Eliza Hall Institute of Medical Research

Improving the efficacy of targeted anti-cancer therapies: potential roles for high grade epithelial ovarian cancer

04/08/2011

Professor Shaun Jackson

Australian Centre for Blood Diseases, Monash University

What drags neutrophils to sites of vascular injury?

11/08/2011

Professor Len Harrison

Walter and Eliza Hall Institute of Medical Research

Immunity, like life is all about regulation

18/08/2011

Dr Guiying Nie

Head, Implantation and Placental Development Laboratory, Prince Henry's Institute of Medical Research

Proprotein convertase 6: critical role in establishing pregnancy and clinical implications

25/08/2011

Emeritus Professor Bruce Tonge

Head, School of Psychology and Psychiatry and Head, Discipline of Psychological Medicine, Monash University

Outcome and Predictors of Youth Depression

01/09/2011

Professor Roger Smith

Director, Mothers and Babies Research Centre/ Endocrine Unit, John Hunter Hospital & Faculty of Health, The University of Newcastle

Humans go viral

08/09/2011

Andrew McCallum

Manager, Commercialisation Services, Prince Henry's Institute

Intellectual Property

09/11/2011

Dr Ben Croker

Laboratory Head, ARC QEII Fellow, Inflammation Division, Walter and Eliza Hall Institute of Medical Research

Genetic analysis of the inflammasome

22/09/2011

VISITING SPEAKERS (CONTINUED)

Associate Professor Ross Lazarus

Director of Bioinformatics, Channing Laboratory

Introduction to Galaxy for Biologists

22/09/2011

Dr Lee Smith

MRC Centre for Reproductive Health, Edinburgh, UK

Androgen Signalling and the Machiavellian Control of Testis Function

29/09/2011

Assistant Professor Tetsuo Maruyama

Department of Obstetrics and Gynaecology, School of Medicine, Keio University

Human uterine stem/progenitor cells: implications for uterine physiology and pathology

06/10/2011

Professor Howard Jacob

Medical College of Wisconsen

Whole Genome Sequencing Just Another Lab Test: The Milwaukee Experience

11/10/2011

Professor Marilyn Renfree

Zoology – University of Melbourne

Marsupials are placental mammals – and lactation specialists

20/10/2011

Dr Marios Stavridis

Centre for Oncology and Molecular Medicine, Division of Medical Sciences, University of Dundee

Signalling interactions controlling pluripotent cell differentiation

21/10/2011

Professor Julie Stout

Director of Research, School of Psychology and Psychiatry, Faculty of Medicine, Nursing and Health Sciences, Monash University

Driving toward treatments for Huntington's Disease: The story of a research movement

27/10/2011

Dr Mike Gate

Medical Research Council, Laboratory of Molecular Biology, Cambridge, United Kingdom

Peptide conjugates of steric blocking oligonucleotides analogues for treatment of Duchenne muscular dystrophy and as microRNA inhibitors

27/10/2011

Dr Darryl Russel

Robinson Institute, Centre for Reproductive Health, School of Paediatrics and Reproductive Health, The University of Adelaide

The cumulus oocyte complex: intelligent packaging for delivery of high competence oocytes

03/11/2011

Dr Matthis Grossman

Department of Medicine and Endocrinology, Austin Health, University of Melbourne

Control of musculoskeletal function and glucose metabolism by androgens in men

10/11/2011

Professor Gary Egan

Director, Monash Biomedical Imaging (MBI), Monash University

Multi-modality biomedical imaging at Monash University: collaborative

17/11/2011

Professor Leendert Looijenga

Translational Patho-Oncology at the Erasmus MC, University Medical Center Rotterdam, The Netherlands

Human maligant germ cell tumors: the ultimate stem cell cancer?

24/11/2011

Professor Axel Themman

Professor in Experimental Endocrinology and Medical Education at the Erasmus University Medical Center Rotterdam, The Netherlands

Anti-mullerian hormone: both regulator and marker of ovarian function

01/12/2011

Professor Joachim L Schultze

LIMES Institute Bonn, Germany

Regulatory T cells: a separate cell type or just a cellular program?

05/12/2011

MIMR POSTGRADUATE COMMITTEE

The MIMR Postgraduate Committee provides support and mentoring for MIMR students and their supervisors, with the aim of ensuring the progress of each student towards the completion of their degree is as seamless as possible.

The committee is made up of a senior staff member and student representative from each centre, and meets monthly to review student progress, discuss details of thesis submission format, postdoctoral training opportunities and any other issues arising from the students' studies.

The committee organises the PhD candidature milestones. In 2012 two new milestones, in addition to confirmation of candidature will be introduced across the University. These will be a mid candidature review and a pre-submission seminar.

In addition to organising the University's formal candidature requirements, professional skills' workshops and social events are also coordinated through the Postgraduate Committee.

The PhD Induction and welcome barbeque in March, the Three Minute Thesis Competition in July and the Postgraduate Symposium for third and fourth-year students in November, all aim to create a nurturing, stimulating and fun environment for students.

In 2011 MIMR had 90 PhD students. 12 students graduated and a further 12 new students enrolled in 2012. For the second year in a row a MIMR student took out the prestigious Mollie Holman Medal for the best PhD thesis in the Faculty of Medicine, Nursing and Health Sciences.

The winner Dr Tony Goldschlager is a neurosurgeon at Monash Medical Centre and was supervised by Professor Graham Jenkin in the Ritchie Centre.

IN 2011 MIMR HAD 90 PHD STUDENTS. 12 STUDENTS GRADUATED AND A FURTHER 12 NEW STUDENTS ENROLLED IN 2012.

Tony's project involved pioneering a new treatment for intervertebral disc disease.

Our postgraduate students were very successful in obtaining postdoctoral fellowship positions, both internationally and nationally, funded from a number of organisations including a CJ Martin postdoctoral fellowship funded by the National Health and Medical Research Council of Australia which was awarded to Dr Bradley Edwards for continuing his studies at Harvard University.

COMMUNITY EDUCATION AND EDUCATION EVENTS

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. In 2011, 9 students spent time in each of the Institute's main research centres and technical facilities, and gained valuable insights into the world of the medical researcher.

Student Open Day 2011

The annual Student Open Day provides undergraduate students with the opportunity to see first-hand the diverse range of research projects on offer at MIMR.

Seventy-two students attended the 2011 Open Day, which was held jointly with Prince Henry's Institute and Southern Clinical School. Evaluation surveys handed out at the conclusion of the Open Day showed that the postgraduate student-led tours were popular, and the researchers were rated as very informative and approachable.

When asked what attracted them to studying at MIMR, students listed cutting-edge technology, good working environment, lab facilities and the research undertaken as their main areas of interest.

Three Minute Thesis Competition

A highlight of the postgraduate calendar, the Three Minute Thesis Competition, challenges PhD students to translate their research from a number of major written papers, into an engaging three minute oral presentation for a lay audience, with the aid of only a single static PowerPoint slide.

Presentations were of an exceptionally high standard and covered a range of research topics including how to save endangered wild cats, finding new therapeutic targets for cancer, optimising the care of preterm babies and pregnant women and how a systems biology genomics approaches will the improve understanding of the innate immunity system.

The winners were:

First Prize:
Samuel Forster CIIID

Second Prize:
Alana Westover TRC

Third Prize:
Lauren Kerr CCR

Postgraduate Student Symposium

The MIMR annual Postgraduate Student Symposium in which all third and fourth year PhD students presented their research projects was held on 23 and 24 November. Designed to improve scientific presentation skills, including the writing of scientific abstracts, and to share the research achievements of our PhD students with the whole MIMR community, the Symposium showcases the critical role of student research to the Institute's success and international reputation.

The event is attended by all MIMR staff and students who provide the students with an opportunity to respond to robust questions. Senior staff and postdoctoral fellows evaluated the presentations and provided the presenters with constructive feedback.

The Symposium prizes were generously sponsored by Life Technologies, who has continued to sponsor these for a number of years. Their representative, Dr Lucy D'Agostino, presented certificates to the winners.

The winners were:

First Prize:
Georgina Ryland CCR

Second Prize:
Rajneesh Verma CRD

Third Prizes:
Agniezka Pindel CCR and
Hazel Tye CIIID

Team Player Awards
(for asking the most questions):
Lisa McKenzie CCR and
Alexander Wilding CCR

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 its 11th year of operation, Andrology Australia continued to build on its strong foundation – establishing new partnerships, piloting education programs, updating its resources, and growing its database of supporters and affiliates. The program remains the peak Australian authority on male reproductive health and continues to garner tremendous support and positive feedback from people who have used its resources and education material. Launched in April 2011, the *Talk about your tackle* campaign was a significant achievement for the Andrology Australia team.

The campaign, which involved a community service announcement for TV and radio, along with a dedicated micro-site, featured former AFL players Matthew 'Richo' Richardson and his father, Alan 'Bull' Richardson. The campaign was subsequently highly commended in the Public Relations Institute of Australia Victoria State Awards.

From 13 to 19 June 2011, International Men's Health Week (IMHW) continues to provide an excellent opportunity to get communities involved in promoting men's health at a grassroots level. Once again, Andrology Australia provided resources to about 1000 individuals and organisations across Australia for men's health events and displays during IMHW.

Andrology Australia Ambassador Merv Hughes also continued to visit regional towns across the country, speaking directly to almost 2000 people about why men should talk more openly about their health.

In addition to encouraging men to look after their reproductive health, the program continues to focus on educating health professionals. In 2011, Andrology Australia piloted a train-the-trainer men's health education program specifically for primary health care nurses, with almost 100 practice nurses participating across 11 (former) Divisions of General Practice.

IN ADDITION TO ENCOURAGING MEN TO LOOK AFTER THEIR REPRODUCTIVE HEALTH, THE PROGRAM CONTINUES TO FOCUS ON EDUCATING HEALTH PROFESSIONALS.

In association with the NSW Multicultural Health Communications Service, Andrology Australia also delivered education to GPs working with Chinese and Vietnamese communities.

This year also saw significant progress in the development of the men's health curriculum framework for medical students, and the completion of a comprehensive male health education module for Aboriginal Health Workers.

For more information about Andrology Australia, please visit **www.andrologyaustralia.org**

2011 GRADUATES

PhD

Lincoln Stamp
Centre for Reproduction and Development

Characterisation of the novel GCTM-5 antigen, its expresiion in human tissue and its use in the isolation of endodermal derivatives from human embryonic stem cells

Cheryl Yin Chih Tay
Centre for Reproduction and Development

Investigating the roles of Sox1 and FEZF2 transcription factors in neural differentiation of human embryonic stem cells

Rebecca Craythorn
Centre for Reproduction and Development and Centre for Women's Health Research

Follistatin isoforms in the female mouse reproductive tract

Charmaine Tan
Centre for Women's Health Research

Epithelial progenitor cells in the human endometrium and endometriosis

Kelly Kenna
The Ritchie Centre

Maternal ethanol consumption in late gestation: effects on vascular physiology in the offspring

Cody Allison
Centre for Innate Immunity and Infectious Diseases

The role of the pathogen recognition molecule, NOD1, in the induction of gastric epithelial cell signalling during helicobacter pylori infection

Ka Yee Fung
Centre for Innate Immunity and Infectious Diseases

Characterization of the novel type I IFN - Ifn-epsilon

Jovana Maksimovic
Centre for Reproduction and Development

Expression and regulation of sialic acid biosynthesis and sialytransferase genes in the mammary gland

Melissa Li-Lian Siew
The Ritchie Centre

Lung aeration at birth

Claire Greenhill
Centre for Innate Immunity and Infectious Diseases

IL-6 trans-signalling modulates TLR4-dependent inflammatory responses via STAT1 and STAT3

Tali Lang
Centre for Innate Immunity and Infectious Diseases

The human hepatitis B e antigen targets and supresses Toll-like receptor signalling pathways

Corey Heffernan
Centre for Reproduction and Development

Transmembrane delivery of specific recombinant proteins for reprogramming of somatic cells and disease therapy

Sean Murphy
The Ritchie Centre

Placental stem cells as a treatment for lung disease

Pinglu (Louie) Ye
CWHR/CURe

Generation and characterisation of a human embryonic stem cell-derived developmental model of the human female reproductive tract epithelium

Georg Schmoelzer
The Ritchie Centre

Monitoring respiratory function during neonatal resuscitation

Badia Barakat
Centre for Reproduction and Development

Investigating the role of activin, inhibin and bone morphogenetic proteins during the first wave of mouse spermatogenesis

BBiomedSc (Hons)

Samantha Barton
The Ritchie Centre

Preventing resuscitation-induced brain injury in preterm lambs

Sambridhi Adhikari
The Ritchie Centre

The role of Activin A in the pathophysiology of Preeclampsia

Shanelle Andrew
The Ritchie Centre

The effect of dummy use on infant arousability: a possible protective mechanism against the sudden infant death syndrome

2011 GRADUATES (CONTINUED)

Steven Cho
Centre for Cancer Research

The role of opioids in the treatment of necrotizing enterocolitis

Justin Lang
The Ritchie Centre

The role of lung aeration in triggering the increase in pulmonary blood flow at birth

Hannah Poole
The Ritchie Centre

Effects of Dummy Sucking During Sleep on Autonomic Cardiovascular Control: Implications for The Sudden Infant Death Syndrome

Hashini Seneviratne
The Ritchie Centre

Characterisation of Telomerase as a Candidate Marker of Endometrial Epithelial Stem/Progenitor Cells

Gavin Brooks
Centre for Innate Immunity and Infectious Diseases

Cytokine Signalling as a molecular bridge between the pathogenesis of Emphysema and Lung Cancer

BBiotech (Hons)

Hilary James Stunden
Centre for Cancer Research

The role of microRNA in the regulation of Nuclear Factor-κB (NF-B) signalling

BMedSc (Hons)

Tommy Supit
The Ritchie Centre

Characterizing placental mesencymal stem cells and tissue response of novel scaffolds for pelvic organ prolapse repair.

BSc (Hons)

Monique Mortale
The Ritchie Centre

IUGR

Khalil Cassimally
The Ritchie Centre

Impact of Dopamine in the preterm infant

MBiomedSci Part 1

Leyla Zaker-Tabrizi
Centre for Innate Immunity and Infectious Diseases

Structure Function Studies of Interferon-Receptor Interactions

Jean Tan
The Ritchie Centre

Role of macrophages in human amnion epithelial cells mediated lung repair

Hadeel Khalil Khayat
Centre for Reproduction and Development

Removal of oncogen c-Myc from the reprogramming cocktail to develop an iPSCs approach for conservation

Catherine Pilapil
The Ritchie Centre

The role of CD4+CD25+Foxp3+ regulatory T cells in human amnion epithelial cell (hAEC) mediated lung repair

Lisa Davis
The Ritchie Centre

Assessment of the behavioural effects of birth asphyxia in spiny mice: relevance to long term outcomes in humans

Rachael Pasco
The Ritchie Centre

In vivo and in vitro development of the spiny mouse embryo

Hemalatha Umapathy
The Ritchie Centre

The role of activated Protein C and IL-37 in pre-term infants with Bronchopulmonary Dysplasia

MRepSci

Gita Pratama
Centre for Reproduction and Development

Characterisation of primary and expanded human amnion epithelial cells for potential cellular therapeutic applications

BA (Hons)

Jessica Anne Gooden
The Ritchie Centre

The impact of sleep-disordered breathing on executive function in children

Emma Owen
The Ritchie Centre

Time course of slow wave activity in children with sleep disordered breathing: A possible mechanism for behavioural deficits

SUPPORTING OUR RESEARCH

Monash Health Translation Precinct Core Facilities
Chief Operating Officer Report
Human Resources
Occupational Health, Safety and the Environment
Logistics
eSolutions Service Centre
Philanthropic Support and Community Engagement
Grant Funding Awarded and Received
Supporters

MONASH HEALTH TRANSLATION PRECINCT CORE FACILITIES

Core Facilities Manager: Dale Cary

The Monash Health Translation Precinct (MHTP) is a partnership between MIMR, Prince Henry's Institute, Monash University and Southern Health's Monash Medical Centre.

This collaboration between researchers and clinicians increases the impact of research through the translation of laboratory findings into improved clinical treatments.

Researchers and clinicians within the MHTP are fortunate to have a broad range of high quality laboratory core facilities that support the precinct's scientific and clinical work.

These facilities are managed by MIMR researchers and staff. Throughout 2010, there was an increase in patronage of all core facilities. During the year all of the microscopes dedicated to the Monash Microimaging Facility were centralised to the 3rd floor of the MIMR building, with the exception of the multi-photon instrument.

The Precinct's core facilities services comprise:

- High Content Screening Facility
- A dedicated satellite Monash Microimaging Facility
- Flow Cytometry Facility
- Histology Facility
- The Monash Medical Centre Animal Facility

MHTP Medical Genomics Facility, comprising the following:

- The Gandel Charitable Trust Sequencing Centre
- ACRF Centre for Cancer Genomic Medicine
- MHTP High Content Screening Centre
- MHTP Microarray Centre

Monash Health Translation Precinct Medical Genomics Facility

Manager: Vivien Vasic

2011 saw expansion of genomic services at the Monash Health Translation Precinct (MHTP) through the establishment of Next Generation Sequencing (NGS) within the new Australian Cancer Research Foundation (ACRF) Centre for Cancer Genomic Medicine.

The ACRF generously provided $1.6 million and together with $169,000 funding from the National Health and Medical Research Council (NHMRC), the latest NGS technologies were purchased. The equipment allows rapid sequencing of entire genomes providing researchers greater insight into the nature of genes involved in cancer. These insights are critical for the development of therapies targeting specific cancers.

ACRF Centre for Cancer Genomics

It was also the year for consolidation of genomic services within the MHTP, with the new ACRF Centre, the well-established Gandel Charitable Trust Sequencing Centre, MHTP High Content Screening Centre and the MHTP Microarray Centre coming together under the "MHTP Medical Genomics Facility".

MONASH HEALTH TRANSLATION PRECINCT CORE FACILITIES (CONTINUED)

Gandel Charitable Trust Sequencing Centre

Providing access to quality DNA sequencing and gene expression technologies, the Gandel Charitable Trust Sequencing Centre services 500 medical researchers and clinicians based at the MHTP as well as nationwide.

These services continued to be in high demand as well as the new Microbial Identification service established through collaboration with Microbiology, Southern Health Pathology the year prior. Using DNA sequencing, the system provides a rapid and accurate method of identifying bacteria and fungi causing disease and illness within 5 hours, improving clinical diagnosis, treatment and care of patients.

MHTP High Content Screening Centre

The MHTP High Content Screening Centre enables researchers to perform medium/large scale cell biology experiments with automation for both experiment set-up and fluorescent microscopic analysis. These enable researchers to perform quantitative studies to examine cellular responses to drugs, cytokines and pathogens.

This facility also contains Dharmacon siRNA libraries that enable inactivation of every gene in the mouse or human genome. In 2011 the centre initiated it's first whole genome siRNA screen; a large experiment where every gene (~20,000) is individually inhibited. This ongoing study has already identified genes potentially involved in cancer drug resistance.

MHTO Microarray Centre

The MHTP Microarray Centre expanded its capacity through an Agilent Technologies Equipment Grant during the year. Microarray technology allows researchers to compare gene expression levels in thousands of genes simultaneously, or simply put, which genes are turned on and off during disease.

In collaboration with Cytogenetics, Southern Health Pathology, the technology has been developed for the provision of Molecular Karyotyping – a powerful tool used to assist clinical investigation of patients with a broad range of developmental disabilities and congenital abnormalities.

Histology Facility

Manager: Lesley Wiadrowski

The Histology Facility supports staff and students within the MHTP and broader research community through the provision of high quality histological services.

2011 continued to see an increase in the volume of work passing through the facility.

We gained several new clients, and the Histology Facility proved to be an important factor in attracting new researchers to the Institute.

The acquisition of new of equipment increased our operating capacity and reduced turnaround times and plans are in place to continue upgrading equipment throughout 2012-13.

Monash Medical Centre Animal Facilities

Manager: Monika Generowicz

2011 was yet another busy year for MMCAF with some interesting challenges thrown into the mix.

On Friday 4 February heavy rainfall and flooding created havoc in many parts of Melbourne, including the MMC site. A late night phone call from a researcher working in B block started a chain reaction of emergency responses from some MMCAF staff who helped mop out flood water from both our B and E block animal facilities.

Unfortunately major equipment housed in the undercroft of E block was submerged (reminiscent of the flood damage from December 2007) resulting in our autoclaves being out of action for the next few months.

Co-ordination, co-operation and lots of hard work by many of the MMCAF staff got us through this trying time.

The influx of researchers moving from the main campus to the Ritchie Centre resulted in a significant increase in the amount of large animal research conducted at B block. As always the E block SPF areas were under constant use and any spare spaces was quickly filled up by new mouse colonies as the needs of our researchers change and grow.

Staffing changes were as always present – Carlie Tobias rejoined the MMCAF team after a serious car accident in 2010 and we welcomed Coral Galea to our Material Support team. Sally-Anne Mason decided motherhood was to be her career choice and Robyn Charman also decided that she needed a career change.

Looking ahead to 2012 we hope for no heavy rainfalls resulting in flooding and equipment outage (twice in 4 years is more than enough) and as always look at ways of improving and expanding our services to the researchers here at MMC whilst dealing with the many smaller challenges that we are faced with on a day to day basis.

CHIEF OPERATING OFFICER REPORT

The role of the Chief Operating Officer at MIMR is to oversee the finance; purchasing and logistics; human resources; occupational health and safety; and general administration roles within the Institute.

We are fortunate these teams are staffed by talented, hard working individuals who all provide vital support to our researchers. These functions have separate reports within this Annual Report.

Financially, it was another stable year for the Institute. We still managed to increase our net revenue despite challenging financial circumstances. We used some of our carry forward reserves to fund a small planned operating loss and it is a credit to our researchers that our competitive research funding remained at a constant level.

Through the Federal Government's Research Infrastructure Support Services (RISS) program, MIMR was awarded funding to set up a Good Manufacturing Practice (GMP) facility for cell based therapies.

The Red Cross is consulting on this project with MIMR and the other initiative partners, including the Royal Children's Hospital and Peter McCallum Cancer Centre. MIMR was also successful in attaining several grants from the Victorian Cancer Agency.

I would like to thank all administrative staff for their hard work throughout the year. I would also like to thank our Director Professor Bryan Williams and the Centre Directors for their ongoing support.

Rod Wealands
Chief Operating Officer

"THROUGH THE FEDERAL GOVERNMENT'S RESEARCH INFRASTRUCTURE SUPPORT SERVICES (RISS) PROGRAM, MIMR WAS AWARDED FUNDING TO SET UP A GOOD MANUFACTURING PRACTICE (GMP) FACILITY FOR CELL BASED THERAPIES."

HUMAN RESOURCES

HR Manager: Tegan McPherson

Human Resources within MIMR focuses on continuous improvement of HR services to attract, retain and support the talented and committed researchers, staff and students.

Throughout the year, a strong demand for staff administration continued, with more than 35 new appointments and more than 120 reappointments. This included the transfer of a new Laboratory Group Head and research team to The Ritchie Centre and the recruitment of a new Laboratory Group Head to the Centre for Reproduction and Development.

We also acquired two new teams to the Centre for Cancer Research including the Monash Comprehensive Cancer Consortium (MCCC) and the Australian and New Zealand Children's Haematology/ Oncology Group (ANZCHOG).

MIMR's Research Centres continued to attract an increased number of international appointments, visitors, honoraries and affiliations, which, in turn strengthens the Institute's innovative research environment.

In March, Melanie Varcoe was welcomed to the HR team to help support the Institute's continued growth.

This year we administered a Staff Attitude Survey and the findings reflected some positive results surrounding teamwork, talent and research. This gave an indication of strong working relationships across the Institute and also respect for the ability and productivity of co-workers.

This survey's results also highlighted that researchers felt supported to achieve research goals and encouraged to actively engage in collaborative research.

As part of key streamlining activities associated with administrative processes, a new electronic timesheet system was implemented. This new system has simplified and shortened casual staff timesheet approval and processing and has significantly reduced the amount of paper used for this process.

Ongoing improvement activities will continue into 2012 with the aim of easing the researchers' administrative workload.

OCCUPATIONAL HEALTH, SAFETY AND THE ENVIRONMENT

Manager: Ganeema Tokhi

Occupational Health, Safety and Environment (OHSE) is an integral component of the Institute's research and management activities.

The Institute's aim is to provide the highest standards of compliance with all relevant OHS legislations and Monash Universities policies and procedures and to provide staff, students, visitors and contractors, the highest level of protection for health and safety that is reasonably practicable in the workplace.

The Institute's OHSE management system fosters a cooperative and a consultative process on workplace health and safety.

OHSE data over the past five years has supported a culture of continuous improvements to minimise incidents and hazards in the workplace. This is reflected in the higher profile that OHSE issues now have at a senior level.

The Institute has achieved compliance in new staff and student safety induction programs. To achieve 100% attendance in 2011, monthly induction sessions and any ad hoc sessions as required were scheduled.

The positive performance indicators provide a clear picture of the achievements in sustained improvements over the recent years.

In the past few years the number of reported incidents and hazards continued to fall. The reduction in the reported hazards and incidents over the past years can be attributed to employees pro-actively and promptly identifying potential issues and hazards before an incident can occur.

This, in turn, can be partially attributed to monitoring and enforcing compliance through biannual workplace safety inspections, requirement attendance of all new employees at regular safety induction sessions and at on-site OH&S training sessions.

Additionally in 2011, the Institute complied with the annual targeted number of two evacuation drills, four OHSE Committee meetings and two workplace inspections.

LOGISTICS

P2P- Purchasing to Payments Manager: Rod Gillett

The P2P team as it is known commonly as, looks after the day-to-day running of the Institutes and supports the needs of researchers and staff.

Tasks undertaken include asset management, laboratory moves, coordinating incoming and outgoing goods, contracts, purchasing, mail just to name a few.

2011 was the year of change for MIMR administration areas. The major change was the Logistics team was abolished and the Finance teams evolved.

The team grew from four to six due to the extra purchasing and finance roles required in the team, which now also includes Southern Clinical School. This was also driven by our large store that can accommodate the extra School.

The main store was busy receiving more then 6500 deliveries for the year from over 5000 Purchase orders for 2011.

Ordering also changed to an altered online form via ESS. This also allowed better reporting back to HOD and streamlined requests and approvals.

While 2011 was very a busy year it was also a successful and satisfying one.

eSOLUTIONS SERVICE CENTRE

Team Leader: Kristian Goree

In 2011 as part of the shared services project, Technology Services Group (TSG), Southern Regional became part of the Universities central IT support department, eSolutions.

As with HR, Research and Revenue, and the P2P hubs Service Centre MMC now reports centrally administratively while still providing the same 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.

A major project for 2011 was the network migration from Novell to a Microsoft network for users university wide. This provided staff with a more stable and robust environment for storage of and accessing data, delivery of applications, and security of information.

PHILANTHROPIC SUPPORT AND COMMUNITY ENGAGEMENT

Support from the community is incredibly important to MIMR, enabling us to pioneer innovative research projects, ensure our facilities and technology is at the cutting edge, and helping support the careers of students and researchers.

We would like to extend our sincere thanks to all the individuals, philanthropic trusts and foundations, corporate donors and sponsors who support MIMR.

Staff Philanthropy

To mark the Institute's 20th Anniversary we launched our first ever staff philanthropy initiative. The MIMR Training and Education Fund was established to provide support for staff, students and researchers within the Institute to develop their careers. All our staff members were asked to donate to this special fund.

The funds raised in the first year enabled us to provide four people with education and training grants which will allow them to attend conferences or travel overseas during 2012 to expand on their research collaborations.

The great response to the campaign shows the commitment of our people to supporting the Institute and we plan to continue this initiative in the years to come.

Patrons Club

The Patrons Club recognises donors who make an annual gift of $1,000 or more to MIMR. Our annual Patrons event this year took place in August and was hosted by Chair of the Patrons Club, Mr Robert Smorgon AM and his wife Mrs Vicki Smorgon.

The event provided Patrons with the opportunity to learn about the groundbreaking work taking place throughout the Institute.

Researchers and students from each of our four Centres gave presentations and provided donors with behind-the-scenes tours of our research laboratories.

This annual event provides an occasion to recognise and thank our significant donors. We are grateful to Robert and Vicki Smorgon for their continuing support of the Institute and the Patrons Club.

2011 Ron Evans Golf Day

The annual Ron Evans Golf Day honours businessman, sportsman, and philanthropist Ron Evans AM, and raises money for the Institute's bowel cancer research program.

2011 was our fifth event and again proved to be a great success with over 100 players competing on the prestigious Royal Melbourne Golf Course – just weeks after it played host to the President's Cup. After a day on the course players enjoyed dinner and supported MIMR even further by bidding for auction items and donating to our research program.

The 2011 Ron Evans Golf Day raised in excess of $140,000 which will further boost MIMR's bowel cancer research and support the Ron Evans Cancer Research Fellowship. Ultimately we hope our research will lead to improvements in the diagnosis and treatment of bowel cancer – the third most common cancer affecting Australian men and women.

We would like to express our sincere thanks to the Evans family for their commitment and generosity to MIMR.

PHILANTHROPIC SUPPORT AND COMMUNITY ENGAGEMENT (CONTINUED)

Community Engagement

MIMR understands the importance of community engagement and the need for general community awareness about the research being conducted at the Institute.

The Institute's Discovery Tours Program is a key way of providing the wider community with an opportunity to meet MIMR's researchers and learn first-hand about our latest research developments.

In 2011, MIMR conducted several Community Organisation presentations where guests from various Probus and Rotary Clubs, RSL, schools and the Association of Country Women of the World learnt about stem cells, women's health, cancer and inflammation, as well as spinal surgery for the elderly.

The Institute is proud of its researchers involved in the CSIRO's Science in Schools program; a program designed to promote science education in primary and secondary schools. Throughout 2011, Drs Maria Liaskos, Ashley Mansell, Tim Moss and Elizabeth Williams all volunteered their time and inspired students to consider a career in medical research.

In September, MIMR researchers gave up their weekend to become 'Inspiring Scientists' at Scienceworks' annual National Science Week event. Over two days, MIMR students, postdoctoral researchers and senior research fellows encouraged hundreds of children to develop an early love for science and scientific research.

The Ritchie Centre hosted two annual public lectures in 2011. The Kaarene Fitzgerald Community Lecture, which focuses on Sudden Infant Death Syndrome research, held in The Ritchie Centre at Southern Health, and its inaugural public health discussion, which this year was the Cerebral Palsy Symposium, held at the BMW Edge Theatre at Federation Square. Both of these events were well attended by both health professionals and the public, and will continue to grow in the coming years.

The Institute also values the importance of the role the media plays in raising awareness of the research being conducted by our scientists. During 2011 the Institute received national and international media attention in particular for its clinical trials on botulinum as a potential cure for asthma and its discovery of how lung cancer can regenerate despite being blasted by chemotherapy.

GRANT FUNDING AWARDED AND RECEIVED

MIMR would like to acknowledge the significant support it receives from the Federal and State Governments, philanthropic trusts and foundations and organisations in Australia and overseas.

We would like to particularly thank the Victorian State Government for its funding of the Institute through the Operational Infrastructure Support Program.

National Health and Medical Research Council (NHMRC)

NHMRC Project Grants

R Ferrero, B Croker

Helicobacter pylori acquisition of host cholesterol: its role in inflammation

2012-14

$403,238

M Gantier

MicroRNA regulation of antiviral responses

2012-14

$483,660

C Gargett, J Werkmeister, A Rosamilia

Tissue engineering a cell-based therapy for pelvic organ prolapse repair

2012-14

$685,920

C Gargett, D Breault

How does endometrium regenerate? Role of epithelial stem/progenitor cells

2012-14

$640,920

R Ghildyal, D Jans, R Tripp, P Bardin

Rhinovirus protease traffic and host factor interactions: translation to prevent asthma exacerbations

2012-14

$562,350

D Gough

Is mitochondrial STAT3 necessary for K-RAS induced myeloid leukemia's?

2012-14

$411,175

T Johns, A Boyd, K MacDonald

An integrated systems biology approach for the development of new therapeutic strategies for the treatment of high grade glioma.

2012-14

$673,520

O Martin, C Sprung, P Lobachevsky

Revealing molecular mechanisms of the synchrotron radiation-induced bystander effect

2012-14

$414,835

T Moss, G Jenkin

Cell therapy for prevention of perinatal inflammation

2012-14

$521,325

GRANT FUNDING AWARDED AND RECEIVED (CONTINUED)

M O'Bryan, L O'Donnell, D de Kretser

Katanin p80 is a key regulator of microtubule dynamics and male fertility.

2012-14

$582,350

D Thorburn, J St John, A Frazier, D Nisbet, S White

Understanding the pathogenesis of mitochondrial disease using iPS cells

2012-14

$618,675

E Wallace, G Drummond, R Lim, M Hearn

Activin mediated endothelial dysfunction: novel therapies for preeclampsia

2012-14

$581,198

F Wong, D Walker, S Miller

Neuro-protection in the Preterm Brain - A New Role for Dopamine Therapy?

2012-14

$521,755

NHMRC Centres for Research Excellence

B Robinson, J Creaney, A Nowak, R Lake, A Musk, B F de St Groth, L Palmer, R Simpson, S Skates, DNWatkins

Centre for Research Excellence in Asbestos Related Diseases

2011-15

$4,500,000

NHMRC Development Grants

P Berger, G Hamilton, M Naughton, B Edwards, S Sands, I Cooke

Development of an effective therapy for Cheyne-Stokes breathing in heart failure

2012-14

$584,700

P Hertzog, M Sullivan

Development of new antivirals

2012-13

$422,418

NHMRC Fellowships

M Tate

NHMRC Peter Doherty Biomedical Fellowship Australia:

Recognition and interaction of virus by the innate immune system

2012-15

$294, 892

D Wu

NHMRC CJ Martin Biomedical Fellowship:

Epistatic and cross-tissue analysis for human gene expression traits

2012-15

$334,884

M Hedger

NHMRC Senior Research Fellowship:

2012-16

$641,855

P Hertzog

NHMRC Senior Principal Research Fellowship (SPRF):

2011-16

$794, 860

F Wong

NHMRC Health Professional Research Fellowship:

Neuro-protection in the preterm brain - A new role for dopamine therapy?

2012-15

$177,448

G Polglase

NHMRC Biomedical Career Development Fellowship:

Unlocking the complexities of postnatal brain injury in preterm neonates

2012-15

$391,076

R Hodges

NHMRC Neil Hamilton Fairley Clinical Fellowship:

Cardiac function in the growth restricted fetus: the effects of betamethasone and melatonin

2012-15

$390,372

Australian Research Council (ARC)

Discovery Grant

R Ferrero, K Stacey

Transport and innate immune properties of DNA in bacterial nano-sized vesicles

2012-14

$270,000

Australian Synchrotron Company Ltd

M Wallace, M Kitchen, M Siew

International Synchrotron Access Program grant

2011

$9,800

GRANT FUNDING AWARDED AND RECEIVED (CONTINUED)

Cancer Australia

C Sprung, P Rogers, D de Kretser

Priority-driven research:

The prediction and treatment of radiation induced fibrosis following cancer radiotherapy

2011-13

$549,000

Commonwealth Government Department of Industry, Innovation, Science, Research and Tertiary Education

Australia-India Strategic Research Fund (AISRF)

P Verma, J Bellare, W Cheng, K Hourigan, S Jadhev, M Thompson

Engineering a novel bioreactor and cell sorter or pluripotent stem cell culture

2011-14

$299,539

Therapeutic Innovation Australia

MIMR Awardees

E Wallace, G Jenkin, C Gargett

Education Investment Fund - SuperScience Translating Health Discovery Project:

Victorian Consortium for Cell Based Therapies (VCCT) - to develop a GMP facility for cell-based therapies

2011-13

$2,000,000

Health Research Council of New Zealand

L Bennet, A Gunn, M Fraser, S Miller, G Jenkin, E Wallace, S Hooper

Can Pluripotent Amnion Epithelial Cells help the Injured Preterm Brain?

2012-14

$504,402 NZD

National Institutes of Health (NIH), USA

C Sprung

High-Throughput Minimally-Invasive Radiation Biodosimetry

2011-12

$151,544

US Department of Defense

C Gargett, J Werkmeister, A Rosamilia, S Edwards

SMART Scholarship:

Novel MSC and scaffolds for regenerating the pelvic floor

2011-13

$108,000

Victorian Cancer Agency (VCA)

Early Career Seed Grants

J Donoghue, T Johns

The anti tumor activity of AMG706 in glioma cell lines and xenografts alone or in combination with panitinumab and AMG102

2011

$99,824

J Cain, DN Watkins

Development of a new biomarker of Hedghog pathway activity in cancer

2011-12

$88,400

M Van Sinderen, T Johns

Novel therapeutic strategies for high grade flioma

2011-12

$93,600

Clinical Research Fellowship

B Markman

The role of the notch pathway ligand DLL4 in lung cancer

2011-12

$400,000

Australian Cystic Fibrosis Research Trust

D Parsons, A Fouras, K Siu, S Hooper, M Donnelley

Localised detection of early stage Cystic Fibrosis disease via quantitative imaging of lung motion

2011

$110,749

GRANT FUNDING AWARDED AND RECEIVED (CONTINUED)

Cancer Council Victoria

D Miles

Postdoctoral Cancer Research Fellowship:

Defining the genetic basis of testis cancer

2011

$67,508

CASS Foundation Limited

Science and Medicine Grants

D de Kretser, R O'Hehir

The use of follistatin to treat the reperfusion injury in organ transplants

2012

$55,000

C Gargett

Uterine mesenchymal stem cells and novel scaffolds for cell-based therapy of pelvic organ prolapsed

2012

$53,000

Cure Cancer Australia Foundation

Fellowship

J Donoghue

The anti tumor activity of AMG706 in glioma cell lines and xenografts alone or in combination with Panitumumab and AMG102

2012

$89,713

Harold Mitchell Foundation

2011 Post-doctoral Travel Fellowship

M Liaskos

$5,000

2011 Senior PhD Student Travel Fellowship

J Khoo

$5,000

International F. Hoffmann-La Roche Group

Pathology Educational/ Research Grant

N Watkins, V Ganju

Advanced Lung Cancer

2011

$50,000

National Heart Foundation of Australia

Grant-in-Aid

M Castillo-Melendez, C Gargett, D Walker

Endothelial progenitor cells in fetal blood and brain: Role in repair and recovery from developmental brain injury.

2012-13

$130,000

Marian & EH Flack Trust

Equipment grant

S White, P Western, A Notini, J St John, N Watkins, H Dickinson, E Williams, P Hertzog

Purchase of a Light Scanner High Resolution Melting Curve Analysis Instrument

2011

$30,000

Monash IVF Research Foundation

Research Grants

C Gargett, GWeston, L Rombauts

Do endometrial stem/progenitor cells have a role in preparing a receptive endometrium

2011-12

$52,870

D Healy, J Halliday, S Breheny

Damaged uterine receptivity as a cause of prematurity

2011

$50,000

Prostate Cancer Foundation of Australia

New Directions Development Award (NDDA)

E Williams, I Haviv

How do castrate resistant prostate cancer cells escape dormancy

2012-13

$300,000

GRANT FUNDING AWARDED AND RECEIVED (CONTINUED)

The Research Foundation of Cerebral Palsy Alliance

F Wong, S Miller

Investigating Neuroprotective Effects in Hypoxia-ischaemia

2011-12

$40,000

T Yawno, S Miller, E Wallace

Novel cell based therapy for Cerebral Palsy

2011

$68,282

Rebecca L Cooper Medical Research Foundation

Al and Val Rosenstrauss Medical Research Fellowship

G Polglase

2012-15

$400,000

Royal Australasian College of Physicians (RACP)

ResMed Foundation Research Scholarship

M Vandeleur

2012

$30,000

The Asthma Foundation of Victoria

Asthma Victoria - Helen Macpherson Smith Trust

M Tate

The role of innate immune responses during influenza-induced asthma exacerbation

2012

$8,333

Monash University

Monash Infrastructure Research Fund

T Johns

Novel antibodies to C-Met

2011

$50,000

Australian Regenerative Medicine Institute (ARMI) SMART funding

U Manuelpillai, B Tuch

2011

$30,000

Faculty of Medicine Nursing & Health Sciences Strategic Grants

F Wong, A Edwards, S Menahem, A Veldman, D Schranz

Fetal cardiac intervention of congenital heart disease

2012

$54,677

C Nold

Interleukin 37 - From promise to product

2012

$35,000

M Nold

The last white spot on the map of the interleukin 1 family of cytokines: IL-1F10

2012

$14,421

J Ferrand, R Ferrero, D Philpott, T Kufer

Production of tools to study NLRC5 role and expression

2012

$14,200

M Gantier

Investigation of the role of Toll like Receptor 8 in H. pylori-induced gastritis

2011

$15,000

Monash University Larkins Fellowship

M Nold

2011-13

$68,282

Faculty of Medicine Nursing & Health Sciences Bridging Fellowships

G Polglase

2011

$35,000

M Siew

2011

$30,000

M Tate

2011

$30,000

GRANT FUNDING AWARDED AND RECEIVED (CONTINUED)

RESEARCH AGREEMENTS

Tragara Pharmaceuticals Inc (USA)

DN Watkins, L Martelotto

Aquired chemo-resistance in small cell lung cancer: a multi-Kinase inhibitor approach

2011

$80,925

AWARDS

MIMR Highest Profile Publication Award, 2011

L Martelotto

MIMR Postgraduate Symposium

1st prize

G Ryland

2nd Prize

R Verma

3rd prize

A Pindel, H Tye

Team player Awards

L McKenzie, A Wilding

MIMR 3 Minute Thesis Competition

1st Prize

R Galinsky

2nd Prize

A Westover

3rd Prize

L Kerr

Monash University Awards

2011 Mollie Holman Medal, Vice Chancellors Commendation for Doctoral Thesis Excellence

G Schmoelzer

Special Commendation, Vice Chancellor's Award for Excellence in Honours Supervision, 2011

R Horne

Postgraduate Publication Award

H Nguyen

Other Awards

S Ellery

Best Student Poster Prize, Fetal and Neonatal Perinatal Society Meeting, Palm Cove, Australia

2011

D Fernando

BMedSc Medical Science Scholarship, Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG)

M Gantier

Best Paper Prize, 7th Australasian Gene Therapy Society Meeting, Melbourne, 2011

2011 Milstein Travel Award, International Society for Interferon and Cytokine Research (ISICR)

C Gargett

Award for Pioneering Research in Endometriosis, Endometriosis Foundation of America

Research Centre for Reproductive Health (RCRH) Award for Excellence in Reproductive Biology Research, Society for Reproductive Biology

A Irving

2011 Milstein Travel Award, International Society for Interferon and Cytokine Research (ISICR)

B Jenkins

2011 Milstein Travel Award, International Society for Interferon and Cytokine Research (ISICR)

M Kaparakis-Liaskos

Australasian Society of Immunology International Travel award

International Society of Mucosal Immunology Early Career Researcher Travel Award

GRANT FUNDING AWARDED AND RECEIVED (CONTINUED)

J Khoo

2011 Milstein Travel Award, International Society for Interferon and Cytokine Research (ISICR)

E Koulaeva

BMedSc Medical Science Scholarship, Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG)

R Lim

Best Scientific Paper, Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) Annual Scientific Meeting, Melbourne, 2011

New Investigators Award, Open Communications, Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) Annual Scientific Meeting, Melbourne, 2011

L Malaver Ortega

Meat & Livestock Association (MLA) New Scientist Award, Society for Reproductive Biology

N Mangan

2011 Herbert Tabor/Journal of Biochemistry Young Investigator Award, International Society for Interferon and Cytokine Research (ISICR)

A Mansell

2011 European Molecular Biology Organization (EMBO) Short-term Fellowship

A McDougall

First prize, Presentation by a late PhD student, Fetal and Neonatal Workshop of Australia and New Zealand, Hobart, Australia

L Nisbet

New Investigator Award, 23rd Annual meeting of the Australasian Sleep Association, Sydney, 2011

M Nold

2011 Georges-Köhler-Prize, German Society of Immunology (GSI)

C Nold

Christina Fleischmann Memorial Award for Young Women Investigators, International Society for Interferon and Cytokine Research (ISICR)

Gender Equity Travel Support Award of the Women's Leadership & Advancement Scheme, Equity and Diversity Centre, Monash University

A Sadler

2011 Milstein Travel Award, International Society for Interferon and Cytokine Research (ISICR)

S Stifter

2011 Milstein Travel Award, International Society for Interferon and Cytokine Research (ISICR)

M Siew

David Henderson-Smart Travel Scholarship, Perinatal Society of Australia and New Zealand (PSANZ)

M Tate

Commendation , 2011 Victorian Premier's Award for Health and Medical Research

Chancellor's Prize for Excellence in a PhD Thesis, The University of Melbourne

Dean's Prize for Excellence in the PhD Thesis, The University of Melbourne

P Vosdoganes

New Investigator Award, Perinatal Society of Australia and New Zealand (PSANZ), 2011

T Yawno

Tania Gunn Memorial Prize for Best Postdoctoral Oral presentation, Fetal and Neonatal Physiological Society Meeting, Palm Cove, Australia, 2011

S Yiallourou

Travel Award, Australasian Sleep Association World Sleep 2011, Kyoto, Japan, Australasian Sleep Society

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- And others who wish to remain anonymous.

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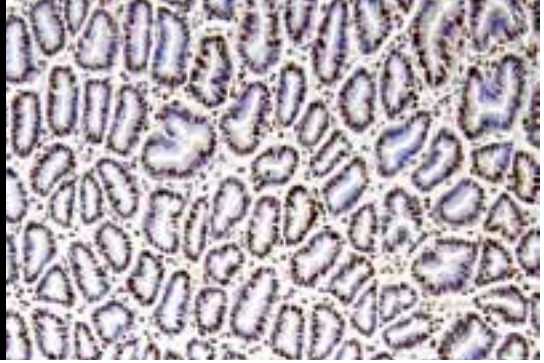
PUBLICATIONS

Editorships
Book Chapters
Journal Articles
Reviews

2011 PUBLICATIONS



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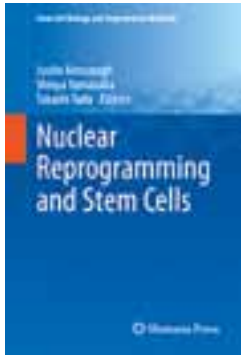

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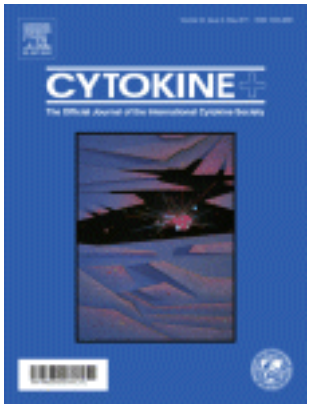

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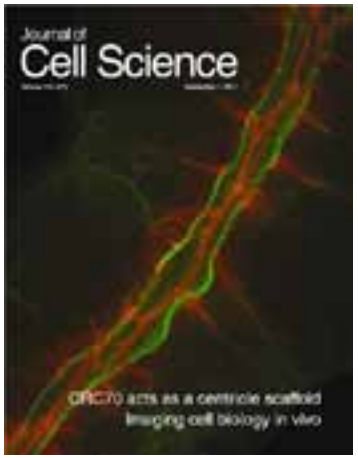

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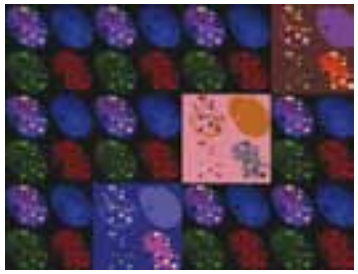

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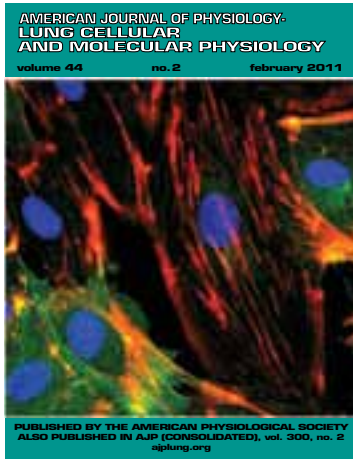

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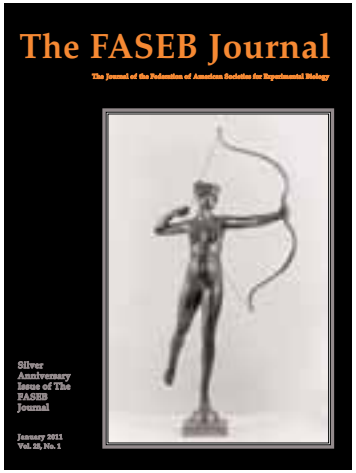

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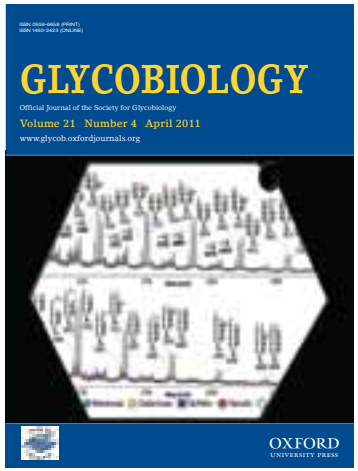

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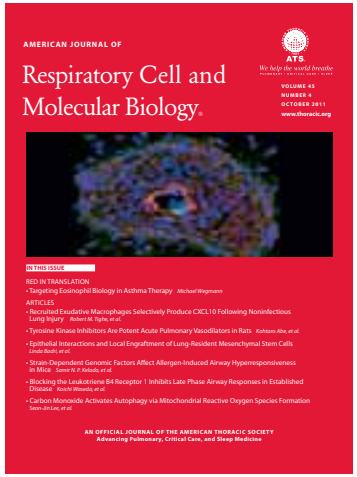

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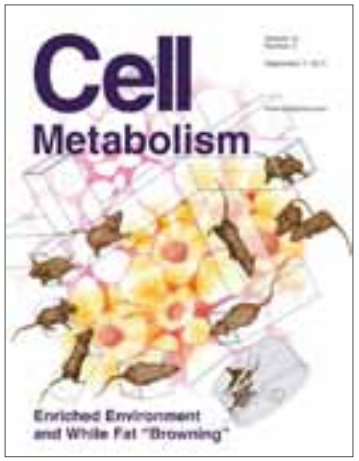

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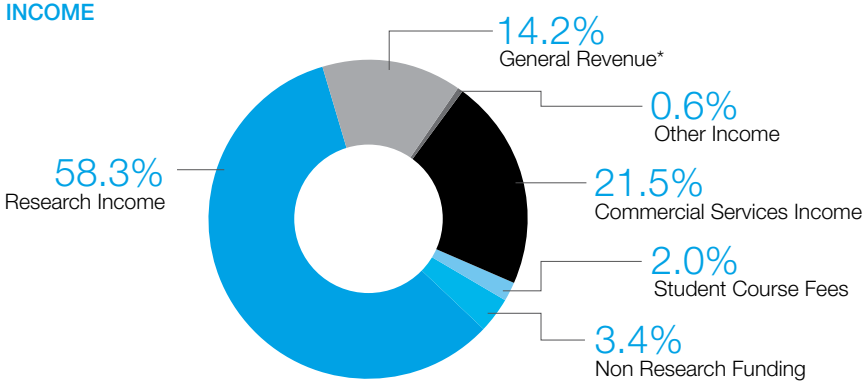
FINANCIAL REPORT

Cash Flow Statement

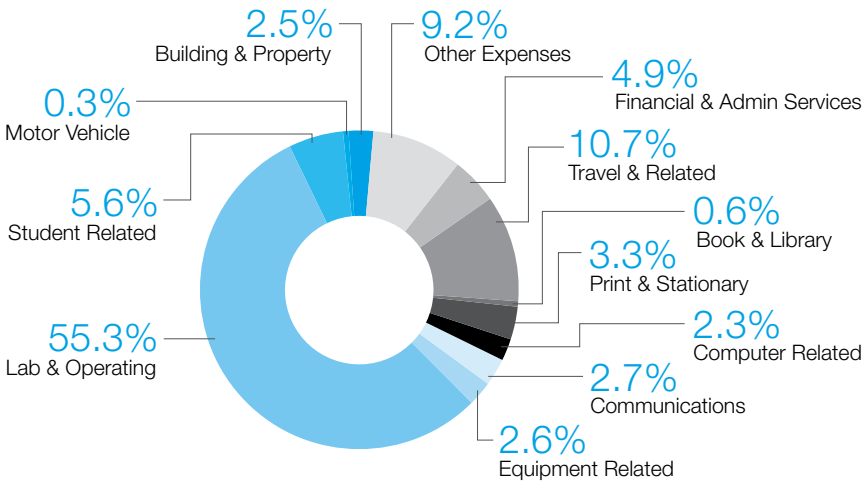
CASH FLOW STATEMENT

YEAR TO DATE 31 DECEMBER 2011

INCOME



NON SALARY EXPENSES



	2011
INCOME	
General Revenue*	3,428,663
Other Income	141,692
Commercial Services Income	5,181,409
Student Course Fees	481,100
Non Research Funding	809,523
Research Income	14,050,286
	24,092,673
SALARIES EXPENDITURE	
All Salary Expenses	15,919,326
	15,919,326
NON SALARY EXPENSES	
Other Expenses	712,438
Financial & Admin Services	381,159
Travel & Related	830,386
Book & Library	47,395
Print & Stationary	253,039
Computer Related	178,259
Communications	206,278
Equipment Related	202,099
Lab & Operating	4,284,478
Student Related	433,742
Motor Vehicle	26,014
Building & Property	193,431
	7,748,718
CAPITAL EXPENDITURE	1,141,778
	1,141,778
OPERATING SURPLUS/DEFICIT**	**-717,149**

** Includes Victorian Government Operational Infrastructure Support Funding*

*** This deficit is due to significant carried forward funds which has offset this small operating loss.*

Design: Dynamic Creations

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