THE ROBINSON INSTITUTE

Annual Report 2009

Australian Research Centre for Health of Women & Babies

Research Centre for Early Origins of Health & Disease

Research Centre for Reproductive Health

Centre for Stem Cell Research

Robinson Institute

THE UNIVERSITY OF ADELAIDE AUSTRALIA

SUB CRUCE LUMEN

Life Impact | The University of Adelaide

WHO WE ARE

Named after renowned obstetrician Professor Jeffrey Robinson CBE, Emeritus Professor at the University of Adelaide, the Robinson Institute brings together a unique blend of clinical, scientific and research leaders with wide-ranging expertise, from epidemiology through to genetics and molecular biology.

Led by reproductive medicine expert Professor Robert Norman, the Robinson Institute was officially launched in March 2009, and consists of more than 350 researchers and students. The Institute incorporates four of the University of Adelaide's leading research centres:

- Australian Research Centre for Health of Women and Babies
- Research Centre for Early Origins of Health and Disease
- Research Centre for Reproductive Health
- Centre for Stem Cell Research

The research of the Robinson Institute concentrates on fundamental clinical and scientific discoveries, with the aim of changing human health and conquering disease. By focusing on the earliest stages of life, the Institute is seeking to prevent disease and promote health in children and adults across generations.

One of the great strengths of the Robinson Institute is the way it links clinicians and researchers from a wide range of disciplines and organisations. This is further enhanced by the Institute's close association with South Australia's health system, which ensures the Institute is linking real data and research with meaningful outcomes for the benefit of the community.

Researchers of the Robinson Institute are based at several sites, including:

- The University of Adelaide
- Women's and Children's Hospital
- Royal Adelaide Hospital
- The Queen Elizabeth Hospital
- Lyell McEwin Hospital
- SA Pathology
- Hanson Institute

Front cover: Izza Tan
Opposite page: Dr Prabha Andraweera

OUR RESEARCH

HEALTH OF WOMEN & BABIES

- Preconceptual Care
- Nutrition and Health Outcomes
- Maternal Health in Pregnancy
- Fetal Growth and Wellbeing
- Intrapartum Care
- Postnatal Health and Wellbeing
- Early Childhood Development related to Maternal Perinatal Care
- Developmental Origins of Adult Diseases

REPRODUCTIVE HEALTH

- Ovarian and Follicular Function
- Oocyte and Early Embryo Development
- Uterine Biology
- Embryo Implantation and Placental Development
- Male Reproduction
- Reproductive Immunology
- Human and Animal Reproductive Biotechnology
- Nutrition, Environment and Reproduction
- Health and Social Outcomes in Reproduction
- Early Life Programming of Fetal Development and Adult Health
- Menopause
- Contraception
- Cancers of the Reproductive System

ORIGINS OF HEALTH & DISEASE

- Early Origins of Health and Disease
- Life Course and Intergenerational Health
- Pregnancy and Development
- Neuromotor Plasticity and Development (NeuroPAD)

REGENERATIVE MEDICINE

- Stroke
- Cardiac Repair
- Tissue Repair
- Blood Disorders
- Cystic Fibrosis and Other Inherited Disorders
- Immune Diseases
- Transplantation Research
- Developmental Biology

CHAIRMAN'S REPORT

Mr Mark Coleman

I have indeed been fortunate to be given the opportunity to be the first Chair of the Robinson Institute Board of Governors. We have an enthusiastic and committed Board who support a very important agenda – research across the life spectrum, from preconception to mature age.

The Institute has been built on the already established research programs of the University of Adelaide, primarily in the areas of reproductive health and regenerative medicine. These programs are recognised internationally in the scientific community for their quality and relevance.

The Board of Governors was first brought together in early 2009 with the primary role of providing advice on Institute governance and key strategic activities. Throughout the year the Board, in collaboration with the Institute Director and Manager, established an Institute Strategic Plan for 2010-2013. This strategy articulates four key objectives for the Institute:

- To attain an outstanding research profile, nationally and internationally in the research sector, government and across the community
- To achieve and maintain a strong funding base to ensure and expand the Institute's operational and research activities
- To attract, retain and develop high quality staff and students to contribute to the Institute's research areas
- To create a dynamic working environment that supports and stimulates success

The achievement of these objectives will maintain and further build a thriving, internationally competitive, and sustainable research institution.

In the year since its establishment, we have already seen some outstanding achievements from the researchers of the Robinson Institute. These have included the wonderful recognition they received at the 2009 South Australian Science Excellence Awards, with Institute Director Professor Rob Norman named SA Scientist of the Year, and three other awards made to researchers of the Institute.

The establishment of the Robinson Foundation in 2009 was also a significant achievement for the Institute. The Foundation could not have been established without the important contribution and commitment of the Steering Group (all of whom are members of the inaugural Foundation Board). We are grateful for their support, which will be invaluable in strengthening the Institute's links with the community. We also welcome His Excellency Rear Admiral Kevin Scarce AC CSC RANR, Governor of South Australia, and Mrs Liz Scarce as joint patrons of the Foundation.

While challenges lie ahead, with great competition in the research environment and the changing health sector both in South Australia and nationally, I am confident the Robinson Institute will continue to build an outstanding research profile through conducting high quality medical research that provides significant health benefits for the wider community.

Finally, I would like to acknowledge and thank for their contributions my colleague members of the Board of Governors, Director Professor Robert Norman, Manager Jo Close, Institute Centre Directors, and Institute researchers and staff.

DIRECTOR'S REPORT

Professor Robert Norman

The formation of the Robinson Institute at the University of Adelaide is a confident statement of our continuing commitment to high impact research, outstanding educational experiences, and quality clinical services that transform the lives of people around the world. The Institute has outstanding research complemented by a strong track record of commercial activity and translational science.

We now have researchers in areas ranging from cellular and molecular biology through to epidemiology, public health and health services research. These researchers continue to have an impact on their fields as judged by inputs (grants, recruitment and new staff) and outputs (publications, high impact research, translation to clinical outcomes, public policies and guidelines).

We have a range of skills in reproductive health and regenerative medicine that is virtually unequalled in one institute anywhere in the world. The main challenge to date has been to bring these unique capabilities together to achieve effective collaboration, communication and a common vision.

Institute Strategies

- **Outstanding Research Profile**
- **Strong Funding Base**
- **Quality Staff & Students**
- **Dynamic Working Environment**

This has been achieved by working from the grassroots to understand the needs of our researchers, through new and innovative collaborative ventures and a shared longer-range strategy for all to contribute to.

As Director, I have been very well supported by an outstanding Board who have provided valuable advice on many occasions. We have also been very fortunate to attract a dynamic support team to drive and implement our ambitious agenda.

I have had outstanding leadership from Jo Close, our Manager, who is entrepreneurial, innovative and diplomatic in all her activities.

Among their many achievements over the year our professional staff catalysed the formation of the Robinson Foundation, which will be integral in building the research capacity of the Institute and improving our community engagement.

An important development of 2009 was the announcement of the Australian Research Centre for Health of Women and Babies as an official research centre of the Robinson Institute. Led by Professor Caroline Crowther, the Centre is committed to attaining the best health and wellbeing possible for women and their babies through excellence and leadership in research, education and knowledge transfer.

Looking to the future, we want to ensure that we are the leading group in our area in Australia in terms of outputs (e.g publications, grants), that we continue to receive high quality and diversified funding, that we invest in our people so that individuals reach their full potential and finally, and equally importantly, that we have a work environment where the culture is positive and supportive of people's personal growth and development.

We hope to build on our current momentum to achieve a dynamic research environment that contributes significantly to the international research areas of regenerative medicine, reproductive health, origins of diseases and the health of women and babies. Our membership is vital in achieving this vision.

HIGHLIGHTS 2009

Launch of the Robinson Institute

More than 200 people attended the official launch of the Robinson Institute at the Adelaide Convention Centre in March. The Robinson Institute was the first of the University of Adelaide's new research Institutes to be launched.

"The science of the transmission of life - what could be more exciting!" inspired Professor Roger Short, Honorary Professorial Fellow from the University of Melbourne's Faculty of Medicine, in his keynote speech at the launch.

Professor Short went on to explain the unique opportunity South Australia has in leading reproductive research. This was reiterated in a speech by the Honorable John Hill MP, who stated, "I hope and believe that the Robinson Institute can increase this state's contribution and participation in the national intellectual and research agendas."

50 years of O&G at the University of Adelaide

Fifty years of the Department of Obstetrics and Gynaecology at the University of Adelaide was celebrated in July with a black-tie dinner at the Australian Wine Centre. The event, coordinated and hosted by Professor Alastair MacLennan, Head of the Discipline of Obstetrics and Gynaecology, brought together over 150 researchers, clinicians and government representatives.

The audience learnt of the history of the Department of Obstetrics and Gynaecology from those who had been there through its development, from humble beginnings at The Queen Elizabeth Hospital to the now thriving research areas in the Medical School.

New facilities at the Women's and Children's Hospital site

The Robinson Institute's expansion on the Women's and Children's Hospital site provided almost 2000m^2 of additional space for our head office and clinical research teams. The redevelopment of the Norwich Centre has incorporated dedicated clinical trial rooms and testing laboratories and is enabling the Institute to expand its research in these critical areas and engage with the community.

Our researchers recognised

Robinson Institute researchers were recognised for their important contribution to society through numerous public awards in 2009, including South Australian of the Year in Health and Science, South Australian Scientist of the Year, Young Investigator Award, Young Tall Poppy Award, Top 10 Health and Medical Research Projects in Australia and the Science Excellence Award for Excellence in Research for Public Good.

Establishing the Robinson Foundation & Peter Couche Foundation

The Robinson Foundation was established in 2009 to raise important funds to seed new areas of innovative research and to raise public awareness of the clinical and policy benefits from the research of the Institute. The Institute also worked with Mr Peter Couche and Mr Stephen Gerlach to establish the Peter Couche Foundation to support the Stroke Research Program of the Institute's Centre for Stem Cell Research.

BOARD OF GOVERNORS

The Board of Governors provides advice to the Director on the governance and general operations of the Institute. The Board is responsible for:

- strategic oversight
- financial and operational oversight
- compliance and risk management
- decision making and policy formulation
- reporting to the University.

BOARD

Mr Mark Coleman
Chairman

Professor Justin Beilby
Executive Dean, Faculty of Health Sciences
The University of Adelaide

Professor Mike Brooks
Deputy Vice-Chancellor & Vice President (Research)
The University of Adelaide

Professor Marie Dziadek
Conjoint Professor
University of New South Wales

Professor Jock Findlay
Senior Principal NHMRC Research Fellow
Prince Henry's Institute of Medical Research

Professor Tanya Monro
Director, Institute for Photonics & Advanced Sensing
The University of Adelaide

Professor Jonathan Morris
Discipline Head, Obstetrics, Gynaecology and Neonatology
University of Sydney

Mr Phil Robinson
Executive Director
Clinical Governance Education & Research
Children, Youth and Women's Health Service

Professor Paul Rolan
Discipline of Pharmacology, School of Medical Sciences
The University of Adelaide

Professor Bik To
Head of Haematology, SA Pathology

MANAGEMENT COMMITTEE

The Management Committee advises the Director on development and implementation of the strategic plan, strategic priority setting, the facilitation of research collaboration, performance management and risk management, and the implementation and delivery of the strategic plan and outcomes, including co-ordination and linkage of research centre activities.

COMMITTEE

Professor Robert Norman
Director, the Robinson Institute

Ms Jo Close
Manager, the Robinson Institute

Associate Professor Jeremy Thompson
Co-Director, Research Centre for Reproductive Health

Professor Sarah Robertson
Co-Director, Research Centre for Reproductive Health

Professor Julie Owens
Co-Director, Research Centre for Early Origins of Health and Disease;
Head, School of Paediatrics and Reproductive Health

Associate Professor Michael Davies
Co-Director, Research Centre for Early Origins of Health and Disease

Associate Professor Michael Ridding
Co-Director, Research Centre for Early Origins of Health and Disease

Associate Professor Mark Nottle
Co-Director, Centre for Stem Cell Research

Associate Professor Stan Gronthos
Co-Director, Centre for Stem Cell Research

Professor Caroline Crowther
Director, Australian Research Centre for Health of Women and Babies

CORPORATE REPORT

Resources

The Robinson Institute is steadily expanding its research capacity and its footprint. The year saw the development of new laboratory and clinical research facilities, the establishment of a head office and support team, and the commissioning of additional core facilities. Researcher numbers continue to expand with the growth of research teams and an ongoing commitment to the training of undergraduate and postgraduate students.

Institute Support Team

In 2009 the Robinson Institute established its support team, which is driving the implementation of Institute strategy, supporting the research directions of our four Centres and their research teams, and ensuring our visibility as an international competitive research group. This small team delivers wide ranging services to Institute members and our stakeholders, from providing support for the attraction of research and infrastructure funding and driving new initiatives supporting collaborative projects, to facilitating professional development for researchers and communicating research findings to the wider public.

Research Facilities

Researchers of the Institute are located across a number of sites: the Medical School of the University of Adelaide's main campus, Women's and Children's Hospital, The Queen Elizabeth Hospital, Royal Adelaide Hospital and SA Pathology. In 2009 two major building projects commenced to expand our capacity on the Women's and Children's Hospital site and expand to a new site at the Lyell McEwin Hospital.

Expansion on the Women's & Children's Hospital Site

One of the key strengths of our research at the Robinson Institute is the integration with clinical services to achieve translational research outcomes. This is particularly apparent on the Women's and Children's Hospital site in North Adelaide. The Australian Research Centre for Health of Women and Babies is at the forefront of clinical research, generating high quality evidence and ensuring findings are incorporated into health care practice.

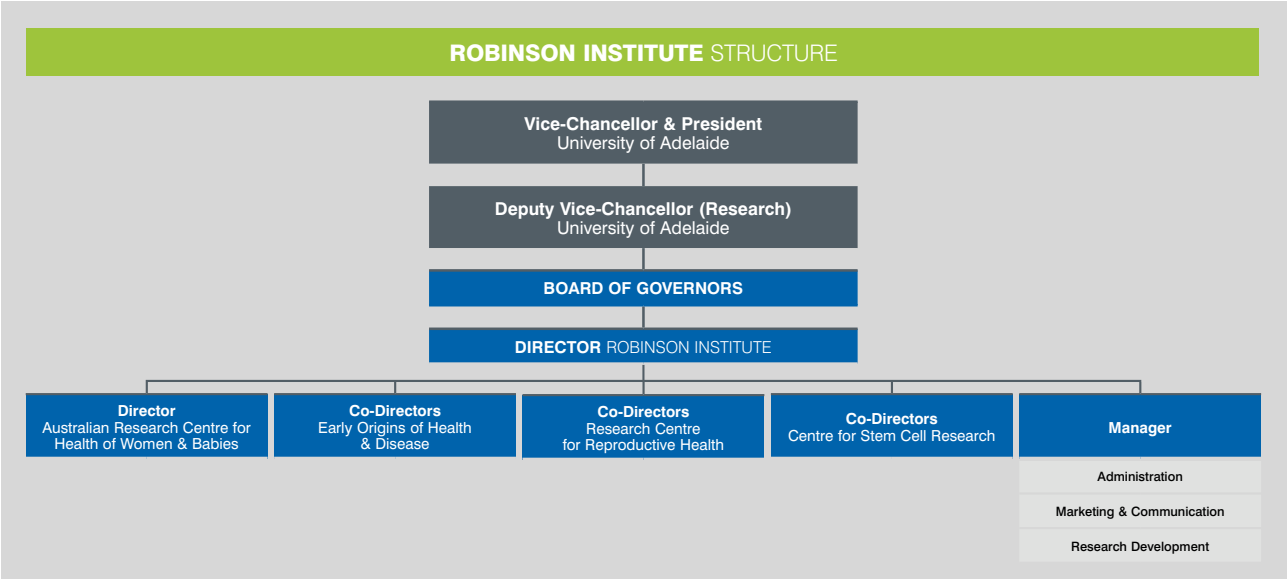
Our expansion on the Women's and Children's Hospital site in 2009 has provided almost 2000m^2 of additional space for the Robinson Institute for our head office and clinical research teams. As well as our clinical and office space within the hospital, we now occupy almost three floors of the Norwich Centre, located directly across the road, where we have access to patients and clinical facilities.

The redevelopment of the Norwich Centre has incorporated dedicated clinical trial rooms and testing laboratories and is enabling the Institute to expand its research in these critical areas and engage with the community. Further to this, it has provided much needed office accommodation for our researchers and created a home for the Institute's support team.

Establishing Dedicated Research Facilities at the Lyell McEwin Hospital

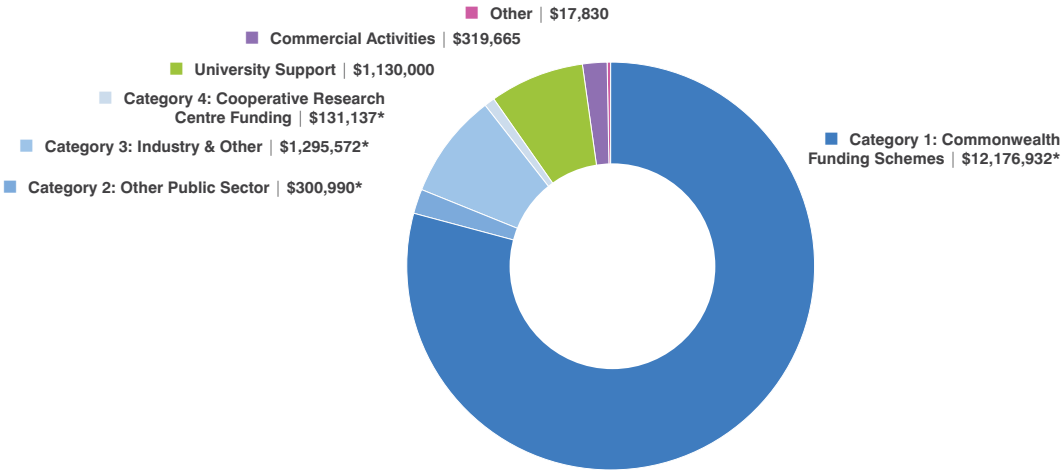
Our integration within hospitals will continue to expand in 2010, when a dedicated research facility is established at the Lyell McEwin Hospital on the northern outskirts of Adelaide. The Robinson Institute's Pregnancy and Development Group, led by Associate Professor Vicki Clifton, will both undertake specific research into understanding the growth and development patterns during pregnancy, while at the same time engaging the clinical community at the hospital in broad ranging research endeavours.

A strength of the Lyell McEwin Hospital is the unique demographic it serves and the large number of patients seen annually. Development on this site is an important commitment by the University of Adelaide to expand its engagement with the health sector.

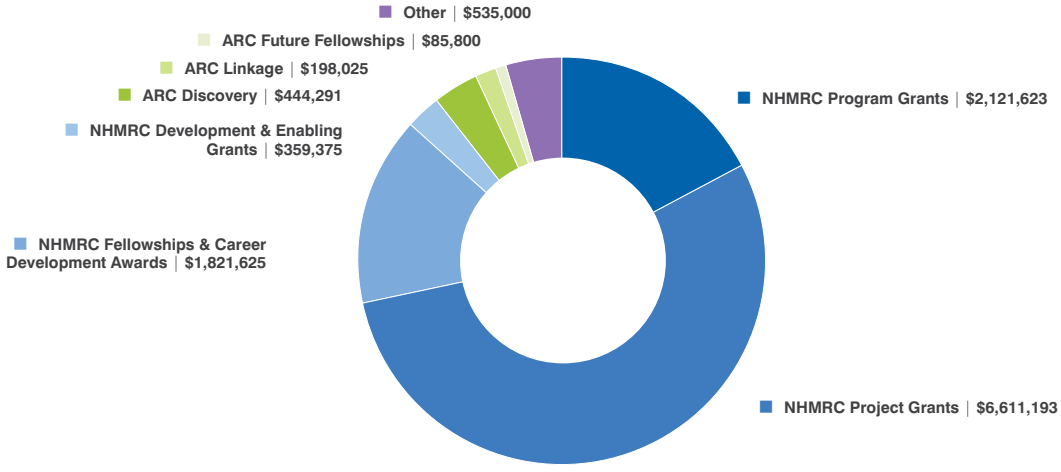


FINANCIALS

2009 | Income $15,372,126



2009 | Robinson Institute Category 1 Income $12,176,932*



** indicative income based upon awarded funding*

COMMERCIAL DEVELOPMENT

In 2009, members of the Robinson Institute generated over $380,000 in contract research and consulting income through relationships with a wide variety of industry partners. This income supplements the extensive competitive grant funding that the Institute attracts and allows researchers to benefit from commercial engagement, intelligence and feedback.

Industry Engagement

A number of researchers in the Robinson Institute continue to engage commercially to translate research developments into practice. Professor Sarah Robertson continues to work with Origio a/s, a Danish company and global leader in Assisted Reproduction Technologies, on a clinical trial to evaluate the use of Granulocyte Macrophage Colony-Stimulating Factor (GMCSF) to improve implantation rates for human embryos produced by IVF. This trial is the world's largest clinical study on IVF media and the interim results of the trial are promising. The work arises from studies into the role of GMCSF on embryos in Professor Robertson's laboratory and a subsequent license agreement with the Danish company Medicult a/s, which became part of the Origio suite of companies.

There is further strong commercial engagement with many researchers in the Robinson Institute including;

- A commercial relationship between Associate Professor David Kennaway and Buhlmann Laboratories involving the supply and use of melatonin antibodies
- A collaborative relationship between Associate Professor Jeremy Thompson, Dr Robert Gilchrist and Cook Medical on technologies to improve the in vitro maturation of oocytes in humans
- A collaborative developmental program investigating the use of IGF-II to improve implantation and placentation, between Associate Professor Claire Roberts and Origio.

Above: Associate Professor Jeremy Thompson

Accelerating the Transfer of Innovations to a Global Market

Several new technologies are now a step closer to market after being awarded funding from Adelaide Research & Innovation's Commercial Accelerator Scheme. Under the scheme, three projects have received significant funding to establish commercial proof-of-concept or reach a development mile stone necessary to attract a commercial partner.

SCOPE

Associate Professor Claire Roberts
$250,000

As part of the SCOPE (Screening for Obstetrics & Pregnancy EndPoints) Program, Institute researchers Professor Gus Dekker and Associate Professor Claire Roberts in the Research Centre for Reproductive Health have identified a suite of genetic markers associated with increased risk of pregnancy complications. The eventual aim of this research is to identify markers that can be used to predict the likelihood of pregnancy complications occurring in first-time mothers, to ensure appropriate care regimes are put in place.

Embryonic Stem Cells

Associate Professor Mark Nottle and Dr Ivan Vassiliev | $179,000

Researchers Associate Professor Mark Nottle and Dr Ivan Vassiliev in the Centre for Stem Cell Research were successful in attracting funding to develop a novel method to isolate embryonic stem cells from mammalian species, which has applications in animal breeding and treatment of human disease.

IVF Vet Solutions

Associate Professor Jeremy Thompson and Dr Robert Gilchrist | $210,000

Funding has been awarded to researchers Associate Professor Jeremy Thompson and Dr Robert Gilchrist to commercially develop new technologies for the in vitro maturation of oocytes. This technology is expected to profoundly improve the in vitro production of animal embryos for primary production industries.

SUPPORTING OUR RESEARCHERS

Research Support played a key role in the Robinson Institute in 2009, facilitating a number of initiatives that enabled research staff to increase their productivity and obtain funding from a wider range of sources.

The Institute sees education as an important growth direction for the future, and will put in place a range of strategies to enable the growth of student and fellow numbers and quality. We intend to provide high profile research opportunities for health professionals and students by identifying research gaps and defining research questions of major importance in reproductive health and regenerative medicine.

Internally, the Robinson Institute offered a number of competitive funding programs to its members:

- Scholarships were awarded to nine of the Institute's Honours students, valued at $4,000 (six scholarships) and $6,000 (three scholarships). The purpose of this program was to attract high quality undergraduate students to the research programs of the Institute, and encourage them in making the transition from undergraduate coursework study to research.
- Five Postgraduate Scholarships were awarded in 2009. This program was aimed at PhD students within the Robinson Institute who were in the first six months of their candidature, with the purpose of attracting and retaining highly quality postgraduate students to the Institute.
- The Robinson Institute also funded six $10,000 Early Career Research Grants, awarded to early and mid career researchers and recent postdoctoral researchers. This program was established in order to promote a continuum of professional growth among Institute members as they progress their research career.

Institute grant provides a head start to early career research

Robinson Institute researcher Agnes Arthur has used funds from a $10,000 Institute grant to further her research into how the body repairs fractured bones. This is a relatively new study, and one of the first in its research field to use human cells.

Agnes works within the Robinson Institute's Centre for Stem Cell Research. Her current study considers how the Eph family of molecules contributes to the interaction between two types of stem cells that are central to the bone repair process: mesenchymal stem cells (located in the bone marrow) and haematopoietic stem cells (located in the blood). Through this focus at the molecular level, Agnes has developed further understanding of how the body's inflammatory response is activated when a bone is broken or fractured.

The funds provided through the Robinson Institute's Early Career Research Grant gave a head start to a highly valuable project, which will potentially lead to the development of new clinical treatments able to assist in the repair of complex fractures and other skeletal trauma.

Recipients of Robinson Institute Internal Funding Programs in 2009

HONOURS SCHOLARSHIPS

Grant Engler | $6,000
Centre for Stem Cell Research

Joshua Fanning | $6,000
Research Centre for Reproductive Health

Kam Panh Troung | $6,000
Centre for Stem Cell Research

Samuel Tim-Ming Lee | $4,000
Research Centre for Reproductive Health

Jessica Laurence | $4,000
Research Centre for Reproductive Health

Nurulaini Abu Shamsi | $4,000
Research Centre for Reproductive Health

Nur Shahrin | $4,000
Centre for Stem Cell Research

Zhu Mao | $4,000
Centre for Stem Cell Research

Noor Lokman | $4,000
Research Centre for Reproductive Health

PHD SCHOLARSHIPS

Lisa Akison | $1,000
Research Centre for Reproductive Health

Wing Hong Vincent Chu | $6,000
Research Centre for Early Origins of Health and Disease

Dale McAninch | $6,000
Centre for Stem Cell Research

Teresa Sadras | $6,000
Centre for Stem Cell Research

Izza Tan | $6,000
Research Centre for Reproductive Health

EARLY CAREER RESEARCH GRANTS

David Mottershead | $10,000
Research Centre for Reproductive Health

David Sharkey | $10,000
Research Centre for Reproductive Health

Michael Stark | $10,000
Research Centre for Early Origins of Health and Disease

Kylie Dunning | $10,000
Research Centre for Reproductive Health

Kathy Gatford | $10,000
Research Centre for Early Origins of Health and Disease

Agnes Arthur | $10,000
Centre for Stem Cell Research

THE ROBINSON FOUNDATION

The Robinson Foundation was established to support the life-giving research of the Robinson Institute, with the principal aim of:

- Raising funds that are needed to seed fund new areas of innovative research, to support the development of our next generation of scientists and to fund special enabling equipment. This will form an integral part of building the capacity of the Robinson Institute.
- Raising public awareness of the clinical and policy benefits of the work of the Robinson Institute in order to enhance the uptake of research findings from the Institute by the community.

The Robinson Foundation will provide opportunities for the Robinson Institute to further engage with the community and to encourage corporate partnerships, volunteering, donations and bequests to support our research.

The Robinson Institute would like to recognise the invaluable support of the inaugural members of the Robinson Foundation, who played a vital role in its establishment and launch. The Institute would like to particularly recognise Ms Mary Patetsos and Mr Ian Nightingale, who spearheaded the initiative.

Founding Members of the Robinson Foundation Board:

Ms Robyn Brown Director, Development & Alumni, The University of Adelaide

Mr Sathish Dasan
Partner, Norman Waterhouse

Mr Richard Fewster

Mr Stephen Gerlach
Chancellor, Flinders University

Mr Tim Hughes Managing Director, Hughes Public Relations

Mr Ian Nightingale Chief Executive, Department of Planning & Local Government

Ms Mary Patetsos Member, various Public Boards and Community Boards of Management

Robinson Foundation Launch Gala Dinner

The Robinson Foundation was officially launched on February 13th 2010 at a gala dinner in the grounds of Government House. The event was hosted by Professor James McWha, Vice-Chancellor and President of the University of Adelaide, in the presence of His Excellency Rear Admiral Kevin Scarce AC CSC RANR, Governor of South Australia.

Ms Cherylee Harris was the Master of Ceremonies for this inaugural event and chef Mr Chris Jarmer catered to the 250 guests. At the dinner, His Excellency and Mrs Liz Scarce were announced as joint patrons of the Robinson Foundation.

The Robinson Foundation would like to recognise the generous support of our key event sponsors:

Event Partner

Festival City Wines & Food, Mr Don Totino

Robinson Foundation

For more information please visit:
www.RobinsonFoundation.org.au

Sponsors

Cleanseas, Totino Estate, Serafino Wines, Novatech, Lush Lighting, Wavals Party Hire, Orlando Wines, Rio Coffee, Anna's Vineyard, Foster's Group, Creative Umbrella

Silent Auction Supporters

Festival City Wines & Food, Vinrock McLaren Vale, Orlando Wines, VIP Home Services, Tomich Wines, De Bortoli Wines, Port Adelaide Football Club, Penfolds, Scarpantoni Wines of McLaren Vale, InterContinental Adelaide, InterContinental Melbourne, Jacob's Creek, Thai Orchid Restaurant, Phil Hoffmann Travel, Haselgrove Wines, Elderton Wines, Fosters Group, Zoos South Australia, Cleanseas, Serafino, Intimo, Port Lincoln Hotel, Telstra, Totino Estate, REX (Regional Express)

PETER COUCHE FOUNDATION

Stroke is the leading cause of disability in Australia, with more than 250,000 people estimated to be living with the aftermath of strokes.

In Australia alone there are 60,000 strokes a year – one stroke every 10 minutes – and it is the country's second greatest killer after coronary heart disease. Furthermore, it is estimated that stroke has a financial burden of $2.1 billion per annum and an immeasurable effect on the afflicted patient and their families.

Mr Peter Couche is a remarkable man who is determined to make a difference for those who have suffered a stroke.

At age 41, Peter was a highly successful stockbroker and father of three, living in London. He suffered an irreversible brain-stem stroke while on a business trip to Singapore. Peter's stroke left him a quadriplegic with "locked-in syndrome". He can't speak and has little muscle control, but has an active and alert brain.

Peter's book, *Lifelines*, records the inspiring story of his struggle for a normal life and documents the hope provided by stem cell therapy. Peter's book is a testament to his strength and determination, having taken 13 years to write.

In association with the Robinson Institute and the University of Adelaide, the Peter Couche Foundation has been established to raise funds to support the Stem Cell for Stroke Research Program of the Robinson Institute. Peter approached the then Chairman of Santos, Mr Stephen Gerlach, in early 2009 about the establishment of such a foundation and both Stephen and Santos have pledged their support and acted as conveners for the Peter Couche Foundation.

A significant challenge is how to repair the brain after damage from stroke and improve its function. This research provides hope for brain repair treatment for stroke-damaged brains. Peter also aims to raise awareness of the incidence and impact of stroke; particularly that useful life does not end just because you have suffered a stroke.

PeterCouche Foundation

For more information please visit:
www.PeterCoucheFoundation.org.au

Like all research, what can be achieved depends on funds raised. Supporting the Stem Cell for Stroke Research Program can provide hope for advancing treatments into brain repair and provide significant benefits to the health and wellbeing of those who have suffered a stroke and their families.

Below: Associate Professor Simon Koblar (Director Stroke Research Program) and Peter Couche

KEY COLLABORATIONS

The Robinson Institute has a number of important collaborative links that are vital in building relationships and the research capacity of the Institute, and improving our networks both with other researchers and the community. Key partners of the Robinson Institute include:

The University of Adelaide

The Robinson Institute is one of the five new research institutes of the University of Adelaide. Within the University the Institute has strong collaborations with the School of Paediatrics and Reproductive Health, the Faculty of Health Science and the Faculty of Sciences. The Robinson Institute has also strengthened its links within the University and some excellent collaborations have come out of non-traditional partner areas including physics and economics.

Hospitals

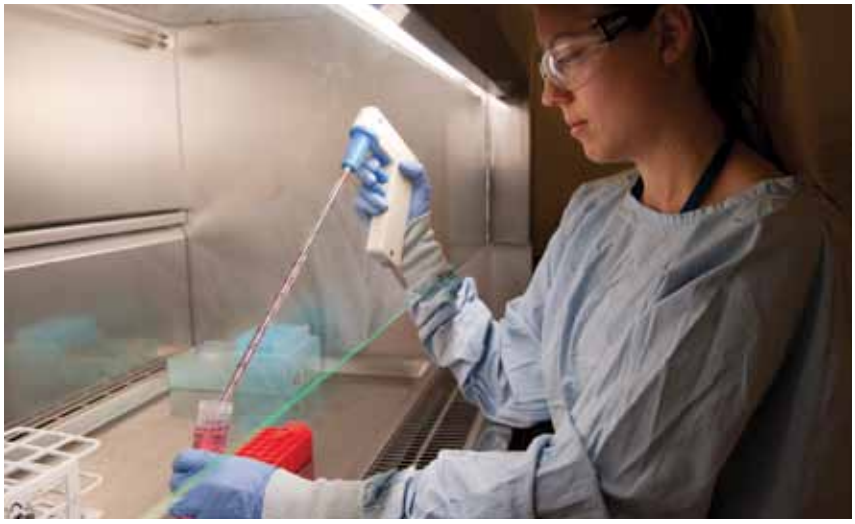
The Robinson Institute and its research centres are embedded in South Australia's health system, with close affiliations existing with the Women's and Children's, Lyell McEwin, The Queen Elizabeth and Royal Adelaide hospitals. This ensures access to clinical material and health policy influence that is unique.

SA Pathology

The Robinson Institute has a strong link to SA Pathology through our Centre for Stem Cell Research.

Women's & Children's Health Research Alliance

The Robinson Institute is party to an ongoing discussion between the Women's and Children's Hospital, Women's and Children's Research Foundation, Women's and Children's Health Research Institute, SA Pathology and other research groups at the Women's and Children's Hospital. This alliance seeks to improve the research outcomes on the site by ensuring appropriate research facilities and collaborations.



Above: Dr Amanda Highet

Healthy Development Adelaide

Healthy Development Adelaide (HDA) is a Research & Innovation Cluster in South Australia. HDA promotes, facilitates and undertakes research that advances multidisciplinary understanding of healthy development by combining research strengths addressing high priority research issues to ensure the physical, psychological and social health of Australian infants, children and adolescents.

HDA has over 150 members and fosters research in over 20 disciplines across the state with a focus on developing a portfolio for South Australia in developmental health research. HDA crosses many sectors including government, health service, university, allied health, associations, and the general community. In 2009 HDA was the winner of the Excellence in Research Collaboration at the SA Science Excellence Awards.

HDA was established in 2004 as an initiative of the University of Adelaide and is led by Professors Robert Norman (Director of the Robinson Institute), Caroline McMillen (University of South Australia) and Michael Sawyer (University of Adelaide / CYWHS). For more information on HDA and our partners see **www.adelaide.edu.au/hda**

HDA has developed very strong research links within the Robinson Institute, with around 22% of members researching within the areas of reproductive biology through to child health. These research links have enhanced HDA's capacity within these areas.

Children's Research Centre, The University of Adelaide

The Children's Research Centre of the University of Adelaide is an affiliate research centre of the Robinson Institute. The Centre is an innovator in the prevention, treatment and cure of chronic childhood illnesses before they manifest as permanent adult disease.

Based within the Women's and Children's Hospital, the Centre focuses on research into the reversal of childhood diabetes, asthma, cystic fibrosis, allergy, and bone impairment. It also pioneers interventions for sleep, gut, mental health and neurological disorders, and studies the safety of new and existing vaccines.

CASE STUDY

WORKING TOGETHER TO SOLVE THE MYSTERIES OF POLYCYSTIC OVARIAN SYNDROME

In 2009, Professor Helen Teede of the Jean Hailes Foundation for Women's Health, and Professor Rob Norman, Director of the Robinson Institute led an Australian initiative to form a national alliance on Polycystic Ovarian Syndrome (PCOS) and successfully secured considerable government funding to support this initiative over the next three years.

The initiative brings together multidisciplinary clinicians, women with PCOS, researchers and government. The National PCOS Alliance is designed to provide a single voice for Polycystic Ovarian Syndrome and has agreed on a vision to improve the lives of Australian women with PCOS through education, research and evidence based health care.

The initiative worked closely with the Minister for Health and Ageing, Nicola Roxon, and the Australian Government committing to $1,134,000 over three years to fund the National PCOS Alliance, specifically for the development of national evidence-based guidelines in PCOS and to support education and translation for consumers and health care professionals.

PCOS is a debilitating condition affecting 11% of Australian women of reproductive age and 21% of indigenous women. **PCOS is the most common cause of anovulatory infertility. Approximately a quarter of couples requiring IVF therapy have infertility complications related to PCOS.**

Once pregnant, PCOS places women at higher risk of pregnancy-related diabetes and pregnancy complications. Other important long-term implications include a four-seven fold increased risk of diabetes, increased cardiovascular risk factors and increased cardiovascular disease.

Australian research shows that 89% of women with PCOS saw more than one health professional before their diagnosis was made, 49% took longer than six months to have a diagnosis confirmed and 41% were very dissatisfied with the manner in which they were informed of their diagnosis.

The first task for the National PCOS Alliance is the development of the first national, and in many areas, international evidence-based guidelines for diagnosis and care of women with PCOS.

89%

Percentage of women who required multiple visits to a doctor before a positive PCOS diagnosis was made.

49%

Percentage of women who took longer than six months to have their PCOS diagnosis confirmed.

41%

Percentage of women who were very dissatisfied with the manner in which they were informed of their PCOS diagnosis.

KEY AWARDS 2009

Above: Dr Julia Pitcher and team

Researchers from the Robinson Institute were recognised for their important contribution to society through a number of public awards including:

South Australian of the Year Award

Professor Robert Norman, Director of the Robinson Institute, was a dual winner at the South Australian of the Year awards winning both the Health and Science categories. The awards recognise and celebrate the achievements of inspirational South Australians and their significant contribution to the State.

South Australian Science Excellence Awards

Professor Robert Norman was also the 2009 SA Scientist of the Year. Professor Norman is a leader in reproductive health and has been involved in many of the pioneering developments in IVF in Australia.

Professor Alastair MacLennan won the Excellence in Research for Public Good Award. His department is internationally known as the largest and most productive research unit in women's and children's health. Alastair's research focuses on safer births, causes of cerebral palsy, better contraception, and management of menopause.

SA Tall Poppy of the Year

Dr Alice Rumbold was announced the South Australian Young Tall Poppy of the Year. Alice won the award for her research into women's reproductive health problems, particularly among Aboriginal women.

NHMRC Ten of the Best

Dr Julia Pitcher's research linking cognitive outcomes in children born pre-term with impaired motor development was named among the top 10 health and medical research projects in Australia by the National Health and Medical Research Council.

Young Investigator Award

PhD student Ms Alison Care won the Young Investigator Award for shedding new light on why some women are infertile and why some pregnancies end in miscarriage.

The Australian, Emerging Science Leaders

Professor Sarah Robertson was nominated one of the Top 10 Emerging Australian Scientists in the 'Australia's Top 100 Emerging Leaders' feature in the *Weekend Australian Magazine*

2009 CSL Florey Medal

The 2009 CSL Florey Medal was awarded to Professor John Hopwood for his life-long work into the diagnosis and treatment of genetically inherited disorders that affect children with devastating clinical effects leading to progressive destruction of the brain and other organs.

CASE STUDY

CLOSING THE HEALTH GAP – DR ALICE RUMBOLD

Despite improvements in recent decades, Aboriginal women are still suffering serious problems when it comes to their reproductive health, according to South Australia's 2009 Young Tall Poppy of the Year, Dr Alice Rumbold (a senior research fellow in the Discipline of Obstetrics and Gynaecology and the Robinson Institute).

A desire to address inequalities in health has, not surprisingly, resulted in Alice working in Australia's most disadvantaged sector - remote Aboriginal communities. Alice says that indigenous people face health setbacks on a day-to-day basis, with sexually transmitted infections such as gonorrhoea and chlamydia unacceptably high in Aboriginal communities, compounded by other health problems such as diabetes, polycystic ovary syndrome and obesity.

These are all having a marked impact on the reproductive health of Aboriginal women, particularly in pregnancy outcomes. Infertility, pelvic inflammatory disease and ongoing pelvic pain are the end result of these health issues and the tragedy is that most of these conditions are largely preventable.

Alice has spent the past five years working with Aboriginal communities since graduating from the University of Adelaide in 2005 with her PhD. She worked at the Menzies School of Health Research in Darwin for several years, spending weeks at a time in remote Aboriginal communities, gradually building trust and respect among Aboriginal women.

Alice states that "an enormous amount of effort and time is needed to establish a good understanding of Aboriginal culture and to break down the long-term distrust that some of these communities have of researchers."

The upside is that Aboriginal health is a key priority of both sides of politics in Australia and there is a bipartisan commitment to address the appalling inequity. In 2005 the **Close the Gap** campaign was born, calling on federal, state and territory governments to commit to closing the life expectancy gap between Indigenous and non-Indigenous Australians within a generation.

Alice is tackling the problem on several fronts. Her research is helping to pinpoint why there is such a high incidence of reproductive cancers in Indigenous communities and how to better detect and manage sexually transmitted infections in these remote areas.

Alice is also keen to encourage young people that studying science provides them with a lot of scope for many exciting careers, "You can travel the world, mix fieldwork with research and laboratory work, and get the opportunity to make a real difference to individuals and communities."

"You have to put in the time to establish good relationships and sometimes this aspect is not recognised by funding bodies, which are keen to see results as quickly as possible."

Dr Alice Rumbold, 2009 Young Tall Poppy

THE FUTURE

The Robinson Institute will focus on implementing initiatives as outlined in our strategic plan, with the primary objectives being to:

- Maintain and grow our outstanding research profile
- Secure a strong funding base
- Develop and support quality staff and students
- Ensure a dynamic working environment

The Institute will continue to maintain its focus on research into reproductive medicine, women's and children's health, origins of diseases and regenerative medicine. We will ensure our research is widely communicated and translated into improved practice, technologies, guidelines and policy in clinical, public and community health settings.

We will further build our research partnerships and collaborations to ensure our research remains relevant, involves the best researchers and is at the cutting edge of developments.

The Robinson and Peter Couche Foundations will be integral in diversifying our funding base and building the research capacity of the Institute. The Institute will work closely with our Board to establish a strong fundraising and communications plan to ensure we receive positive outcomes from these initiatives.

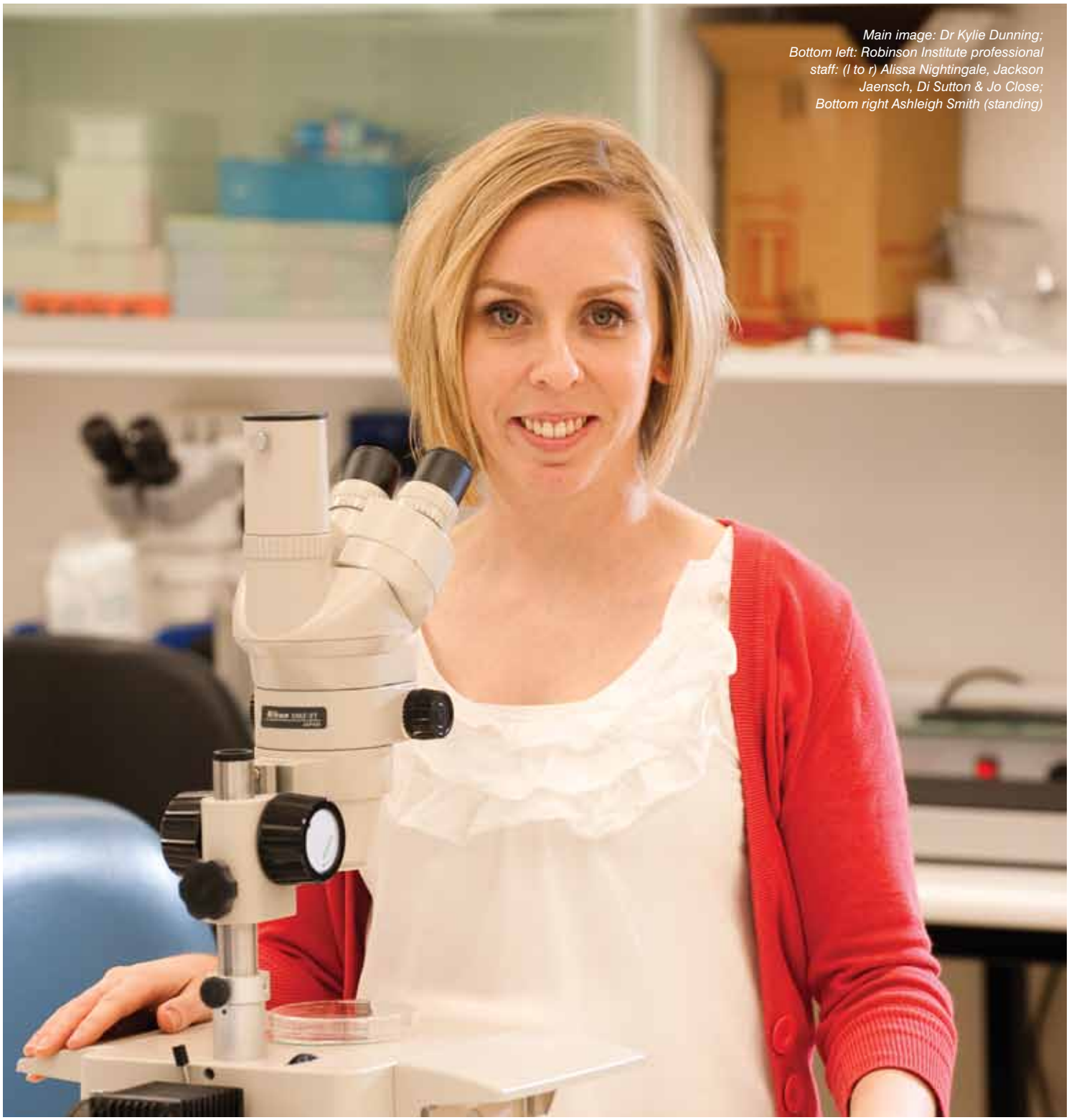
The Institute is working towards increasing collaboration (particularly between our research groups and centres) and finding opportunities to integrate research studies with patients, develop systems and resources for managing data, link clinical studies with epigenetic profiling, assemble significant biobanks and data collections, and generate research findings that could not be obtained without such a multidisciplinary approach.

In 2010 the Institute will work on building a positive working environment for our researchers and students. The Institute will establish mentoring and professional development programs to further develop the skills and capabilities of our researchers

A significant threat to realising the research potential of the Robinson Institute and achieving our vision is providing adequate space and infrastructure to conduct research. Although further infrastructure projects have already commenced, in the future we aim to provide additional infrastructure that will further expand our research horizons.

The Institute has a large and exciting research agenda. We are proud of our achievements to date and look forward to working closer with the research community and wider health sector to ensure our research outcomes are of the highest relevance and importance to the wellbeing of society.

Main image: Dr Kylie Dunning;
Bottom left: Robinson Institute professional staff: (l to r) Alissa Nightingale, Jackson Jaensch, Di Sutton & Jo Close;
Bottom right Ashleigh Smith (standing)



Robinson Institute
ARCH: WOMEN & BABIES HEALTH

THE UNIVERSITY OF ADELAIDE
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AUSTRALIAN RESEARCH CENTRE FOR HEALTH OF WOMEN AND BABIES

Centre Director's Report

The Australian Research Centre for Health of Women and Babies (ARCH) had another tremendously successful year in 2009, with the initiation of new studies, sustained growth and completion of major projects.

All six research divisions within ARCH (Research Synthesis, Clinical Studies and Trials, Translational Health, Indigenous Maternal and Perinatal Health, Research Networks and Education, and International Maternal and Perinatal Health) have seen sustained growth and remained highly productive. During 2009 ARCH became a research centre within the Robinson Institute.

ARCH research leaders and staff provide expertise in research methodologies, maternal and perinatal care, study coordination, dietetics, psychological assessment, data management, statistics, office administration and knowledge translation. The effective partnerships within and between ARCH research divisions are highly valued, as are the high achievements in 2009 of individual staff and students.

ARCH, through its individual studies, collaborative research networks and educational programs, continues to enjoy strong, enduring partnerships with researchers in key institutions and health professionals in participating hospitals providing care for women and their babies within Australia and New Zealand, and further afield.

As we continue to implement our strategic plan initiatives for better health through excellence in leadership, research, education and knowledge translation, we are making meaningful differences for women and babies and their families.

Targeted Research Areas

- Care before, during and after pregnancy and childbirth
- Health care and lifestyle interventions during pregnancy and later health
- Child health after pregnancy and childbirth intervention studies
- Indigenous maternal and perinatal health
- International maternal and perinatal health
- Promoting and supporting evidence-based health care

Centre Director

Professor Caroline Crowther

RESEARCH DIVISIONS

RESEARCH SYNTHESIS

Research Leaders: Professor Caroline Crowther, Professor Jodie Dodd, Ms Philippa Middleton, Dr Rosalie Grivell

The Research Synthesis Division conducts, promotes and supports the preparation and updating of high quality systematic reviews of the existing evidence on questions of relevance to women and babies in Australia, regionally in South East Asia, and internationally.

The Division was successful in securing funding to support the Australasian Review Authors Group for the Cochrane Pregnancy and Childbirth Collaborative Review Group from the commonwealth Department of Health and Ageing for the next three years, 2009-2011.

Funding was obtained through the NHMRC to undertake an individual patient data (IPD) meta-analysis on the use of magnesium sulphate in women at risk of very preterm birth for neuroprotection of the fetus. This patient level analysis will clarify optimal gestational age, timing prior to preterm birth that magnesium sulphate should be given, the best dose and regimen to use, and which women are most likely to benefit. The study titled "Magnesium sulphate in women at risk of preterm birth for fetal neuroprotection – an individual patient data (IPD)" is funded for two years, 2010-2011.

The Division's Australian review authors contributed to 89/324 (28%) of all the Pregnancy and Childbirth reviews and 26/101 (26%) of the protocols published in the Cochrane Library (as of Issue 4, 2009). Over the past year, members of the Cochrane Pregnancy and Childbirth Australian Review Authors Group were involved in preparing 12 titles, 12 protocols, 13 new reviews and 11 updated reviews, considerably exceeding key performance indicators.

The Division actively monitored the progress of over 150 Australian review authors, offering support and encouragement at key stages of review preparation. The ARCH research leaders and other project investigators with grant funding from the Department of Health and Ageing provided intensive support to most protocols, reviews, and updates being prepared for publication and in addition provided substantial support to other Cochrane review groups and to the South East Asia – Optimising Reproductive and Child Health In Developing Countries (SEA-ORCHID) project.

CLINICAL STUDIES AND TRIALS

Research Leaders: Professor Caroline Crowther, Professor Jodie Dodd, Ms Philippa Middleton, Dr Rosalie Grivell, Professor Alastair MacLennan, Dr Bill Hague, E/Professor Jeffrey Robinson, A/Professor Ross Haslam, Dr Andrew McPhee, Dr Chad Andersen

The Clinical Studies and Trials Division conducts, promotes and supports high quality randomised trials and studies, to answer research questions of major importance in maternal and perinatal health, across the spectrum from preconception, through pregnancy and childbirth, infancy and later life, of relevance to women and babies worldwide.

ARCTURUS: Australasian Randomised Collaborative Trials Uniquely aRe Us

Three new research initiatives within the Division are focused around the priority themes of care for women with a high-risk pregnancy to improve health outcomes and care around preterm birth.

A*STEROID: *Australian Antenatal Study To Evaluate the Role of Intramuscular Dexamethasone versus Betamethasone prior to preterm birth to increase survival free of childhood neurosensory disability.*

Both dexamethasone or betamethasone, given to women at risk of preterm birth, substantially improve neonatal and child health. There are conflicting reports as to whether dexamethasone is better than betamethasone. The aims of this randomised trial are to compare the benefits and harms associated with these treatments. This multicentre randomised trial commenced recruiting in 2009, with 13 hospitals participating within Australia by December 2009.

MCA Doppler Study: *Fetal middle cerebral artery Doppler velocimetry to determine the timing of second and subsequent fetal blood transfusions in the treatment of fetal anaemia secondary to red cell alloimmunisation – a randomised controlled trial.*

Red cell alloimmunisation is estimated to affect 0.1% to 0.6% of all live births. Treatment of the resultant fetal anaemia with intrauterine fetal blood transfusion has been associated with survival rates in excess of 90%. However, intrauterine fetal blood sampling and transfusion is an invasive procedure, with recognised serious complications, which may result in the need for early birth and, rarely, mortality. This multicentre trial aims to assess in the fetus where one intrauterine transfusion has been performed for anaemia due to red cell alloimmunisation whether fetal middle cerebral artery (MCA) peak systolic velocity (PSV) can be safely used to determine the timing of second and subsequent fetal blood transfusions without increasing the risk of adverse fetal and neonatal health outcomes.

DIAMIND Study: *Postpartum reminders to test for Type 2 diabetes in women who have experienced gestational diabetes mellitus.*

Women who have had gestational diabetes mellitus may go on to develop Type 2 diabetes. Having blood glucose tests after child-birth is important in preventing or delaying Type 2 diabetes through early identification and management. However what is not known is the best time to do the testing, or the best way of sending reminders to women who require a test. The DIAMIND study is a randomised controlled trial designed to help answer these questions, using mobile phone technology.

Six ongoing major trials/studies coordinated by ARCH

The Division's six ongoing major research studies are evaluating care during pregnancy and childbirth, care around preterm birth and care for women with a multiple pregnancy.

LIMIT: Limiting weight gain in overweight and obese pregnant women to improve pregnancy outcomes: a randomised trial. Obesity is a significant health issue for women during pregnancy and childbirth, with estimates suggesting that over 35% of Australian women aged between 25 and 35 years are overweight or obese. There are well-documented risks associated

with obesity. The aims of this randomised controlled trial are to assess whether the distribution of a package of dietary and lifestyle advice to overweight and obese women during pregnancy to limit weight gain is effective in improving maternal, fetal and infant health outcomes.

IDEAL: Investigation of dietary advice and lifestyle for women with borderline gestational diabetes. Current clinical practice involves the treatment of women with mild gestational diabetes. It is currently unclear whether the benefits of similar treatment for women with more borderline gestational glucose intolerance outweigh any harm. The aims of this randomised clinical trial are to assess whether treatment of dietary and lifestyle advice, given to pregnant women who have borderline glucose intolerance on screening for gestational diabetes, reduces neonatal complications without increasing maternal risks.

PROGRESS: Progesterone after previous preterm birth for the prevention of neonatal respiratory distress syndrome. Respiratory distress syndrome associated with preterm birth is the major cause of early neonatal mortality and morbidity. Amongst survivors, there is considerable risk of chronic lung disease and long-term neurological disability. Progesterone is involved in maintaining uterine quiescence, and its withdrawal leads to the onset of labour. Although recent reports of progesterone supplementation for women at risk of preterm birth show promise, there is currently insufficient data on clinically important outcomes to enable informed decision-making. This large, international randomised trial is evaluating whether antenatal vaginal progesterone for women who have had a previous preterm birth is effective in reducing the risk of subsequent preterm birth and its associated risk of adverse infant health outcomes.

TWINS: Timing of birth at term; a randomised trial. This multicentre randomised trial is evaluating the optimal time of birth for women with an uncomplicated twin pregnancy at 37 weeks gestation.

PPROMT: Preterm prelabour rupture of membranes close to term. This large, multi-national randomised trial is coordinated from the University of Sydney, and is evaluating the optimal time of birth for women with preterm prelabour ruptured membranes between 34 and 37 weeks gestation.

CLOSURE: Skin and subcutaneous fascia closure at caesarean section. This randomised controlled trial is assessing the effects of different methods of skin and subcutaneous fascia closure on maternal wound complication rates. It compares absorbable versus non-absorbable subcuticular suture material for skin closure and closure of subcutaneous fascia versus non-closure.

STARS: Studies, Trials and Assessments after Research Studies

Cerebral Palsy Research Group

The South Australian Cerebral Palsy Research Group continues to lead international research into the causes of cerebral palsy. It has NHMRC funding for its project “Genomic and environmental triggers for cerebral palsy” and has recently been awarded a research grant by the Cerebral Palsy Institute and Foundation of New South Wales.

In the current project, DNA from over 4,000 cases and controls around Australia have been collected using cheek swabs. Large amounts of epidemiological data are being collected from the same pregnancies. New studies are beginning, looking at possible major chromosomal structural changes in cerebral palsy children.

The Cerebral Palsy Research Group has published several novel papers in high impact journals and has presented its research at national and international scientific meetings.

The Group has found significant associations between mutations in genes that control the fetal response to infection and inflammation, and exposure to viruses, particularly of the herpes virus group. These viruses are also associated with increased risk of pregnancy hypertension

and preterm birth. These outcomes are more likely when the fetus is genetically susceptible to infection.

The research group has found common gene mutations (polymorphisms) in babies with cerebral palsy and other mutations that may lead to preterm birth. Very preterm birth may result in brain haemorrhage, secondarily causing cerebral palsy. There appears to be an interaction between environmental risk factors for cerebral palsy, for example, prematurity, infection, chronic growth restriction etc. and cytokine polymorphisms. The latter may increase susceptibility to infection, either by down regulating the normal fetal inflammatory response, making the developing fetal neurons vulnerable to destructive viruses, or by up regulating an excessive cytokine response that can damage the developing brain.

Major Follow-up Studies Underway

The ongoing follow-up of children born following antenatal interventions is essential to understand the longer-term implications of pregnancy care on infant and childhood development. Four key multicentre trials, all funded by NHMRC project grants, are underway:

ACTORDS 6-8 year follow-up: the follow-up of children to early school age to assess the effect of repeat antenatal corticosteroids on childhood growth and development.

ACTOMgSO4: the follow-up of children to early school age to assess the effect of antenatal magnesium sulphate on childhood development.

MiG TOFU: the follow-up of children at early school age to assess the effect of metformin on childhood development.

LIMIT: the follow-up of children at six and 18 months to assess the effect of dietary and lifestyle advice to overweight and obese women during pregnancy to limit weight gain on childhood development.

INDIGENOUS MATERNAL AND PERINATAL HEALTH

Research Leaders: Philippa Middleton, Professor Caroline Crowther, E/Professor Jeffrey Robinson, Dr Alice Rumbold

The Indigenous Maternal and Perinatal Health Division aims to continue to expand its collaborations with Indigenous organisations and communities to conduct research of relevance for Indigenous women and their babies.

In 2009 the Division published the Strategic Health Research Program Report "Preventing infant deaths among Aboriginal and teenage women in South Australia" (**www.adelaide.edu.au/arch**).

The Strategic Health Research Program (SHRP) of the South Australian Department of Health commissioned ARCH to undertake a synthesis of Australian and international research to identify possible reasons for the higher infant and perinatal mortality among Aboriginal and Torres Strait Islander women and teenage women in South Australia; and to identify strategies and models for preventing infant deaths.

The Division also looked at the influence of maternal education and community resilience on infant mortality and identified strategies for reducing unplanned pregnancies among teenage women.

The Strategic Health Research Project titled "Preventing infant deaths among Aboriginal and teenage women in South Australia – a research synthesis" was completed and a final report, written by Ms Philippa Middleton, was submitted to the South Australian Department of Health in December 2009.

Numerous organisations collaborated in this research. The report identified 17 health-related and social factors relevant to Aboriginal and Torres Strait Islander women and teenage women, and with the potential to be modified in order to reduce infant mortality or to reduce or prevent other adverse birth and infant outcomes. These factors were: alcohol use, antenatal care, birth spacing, breastfeeding, diabetes, family violence, home visits, hypertension in pregnancy, infection, nutrition, obesity, poverty, social and emotional wellbeing (SEWB), SIDS/SUDI, smoking, social support and substance use.

The research synthesis shows that many strategies and models may be used effectively to improve health and social outcomes for Aboriginal and teenage mothers and their children in South Australia. These, however, will require consultation with the relevant communities and groups, as well as careful, sensitive and appropriate implementation. Since many health outcomes have their origins in pregnancy or early childhood, an intergenerational perspective is necessary. Preconception and interpregnancy care is a priority, as is care of young women during adolescence and beyond.

INTERNATIONAL MATERNAL AND PERINATAL HEALTH

Research Leaders: Professor Caroline Crowther, Professor Jodie Dodd, Ms Philippa Middleton

The International Maternal and Perinatal Health Division aims to expand its wide collaborative research links within South East Asia and internationally to facilitate maternal and perinatal research, support and education.

SEA-ORCHID: South East Asia – Optimising Reproductive and Child Health in Developing Countries

SEA-ORCHID is an evidence-based care capacity building collaborative project aimed at optimising reproductive health outcomes in South-East Asia. It is funded by the Wellcome Trust and NHMRC.

During 2009 ARCH has actively promoted the results of the project at national and international forums and through publications.

Current and ongoing initiatives

Professor Caroline Crowther was appointed to the advisory board of the Global Health Project–near miss maternal mortality, WHO, Geneva.

Ms Philippa Middleton and Associate Professor Vicki Flenady have been working with the International Stillbirth Alliance (ISA) to synthesise and publish evidence about the epidemiology of stillbirth, interventions to prevent stillbirth and implementation research gaps.

Professor Jodie Dodd has worked towards establishing an international network of maternal fetal medicine specialists willing to collaborate in priority research questions (MCA Doppler Study).

CASE STUDY

CEREBRAL PALSY

Top: Professor Alastair MacLennan
Above: Mr Jimmy Barnes

Research leaders within ARCH have been conducting a number of linked and groundbreaking studies of ways to prevent cerebral palsy.

Cerebral palsy is a childhood disorder where the control of body movements is impaired. One in 500 children born in Australia has cerebral palsy and this rate has not changed in the past 50 years. One-third of children with cerebral palsy are born preterm.

The large Australian and New Zealand magnesium sulphate trial (ACTOMgSO4), led by Professor Caroline Crowther, has provided vital evidence that when mothers are given magnesium sulphate immediately prior to very preterm birth, the risk of the baby dying or having cerebral palsy is significantly reduced. This evidence has subsequently been synthesised and consolidated by a Cochrane systematic review authored by ARCH personnel together with Australian and international colleagues. The Translational Health Division within ARCH has led a 30-member multidisciplinary panel, based on this evidence, to develop guidelines to be used in clinical practice around Australia and New Zealand to reduce cerebral palsy related to preterm birth.

Many human diseases are now thought to be linked to a genetic vulnerability and can be triggered by environmental factors. A research team, led by Professor Alastair MacLennan, is investigating more closely the role of genetics in the development of cerebral palsy. They are testing a new hypothesis that cerebral palsy may be associated with fetal or maternal genetic susceptibility to infection during pregnancy or other environmental hazards.

Our researchers are better understanding the underlying causes of cerebral palsy – the genes that are responsible and the environmental factors that trigger this debilitating disease.

Researchers within ARCH are taking significant steps to preventing or potentially curing cerebral palsy. Soon we may be able to identify pregnancies most at risk, avoid environmental risk factors and develop cures.

1/500

One in 500 children born in Australia has cerebral palsy - a rate unchanged for 50 years.

Above: Professor Jodie Dodd, Professor Caroline Crowther and Ms Philippa Middleton

The International Maternal and Perinatal Health Division's key research strategies are benefiting women and babies worldwide by continuing to:

- Collaborate in international multicentre randomised trials coordinated by other researchers of relevance to women and babies in Australia
- Work towards establishing an international network of maternal fetal medicine specialists willing to collaborate in priority research questions
- Contribute to international medical education
- Lead, and collaborate in, international individual patient data analysis projects
- Provide support to the SEA-ORCHID project and similar initiatives
- Encourage and support new maternal and perinatal research projects within South East Asia
- Provide advice to the World Health Organization (WHO) projects on maternal and fetal health
- Work with the International Stillbirth Alliance (ISA) to synthesise and publish evidence about the epidemiology of stillbirth, interventions to prevent stillbirth and implementation research gaps
- support development of the IMPAC (Integrated Management of Pregnancy and Childbirth) guidelines - "Family and Community Health: Making Pregnancy Safer", WHO, Geneva (Dr Matthews Mathai).

TRANSLATIONAL HEALTH

Research Leaders: Ms Philippa Middleton, Professor Caroline Crowther, Dr Carmel Collins

The Translational Health Division aims to promote evidence-based practice in women's and babies' health by the dissemination and implementation of clinical research findings into clinical practice.

ARCH is a member of the NHMRC Guideline Assessment Register which provides methodological support to groups developing national clinical practice guidelines. Extensive work with the Australian Cancer Network and the NZ Department of Health in helping them update bi-national melanoma guidelines culminated in NHMRC approval in late 2008. These guidelines are anticipated to significantly guide and influence clinical practice internationally.

Philippa Middleton, Rebecca Tooher and Caroline Crowther were awarded NHMRC grants for supporting the development of two guidelines:

- beyondblue: perinatal mental health guidelines - from mid 2008 ARCH has assisted the beyondblue organisation to produce national guidelines for perinatal mental health
- Venous thromboembolism guidelines - ARCH has been appointed by the National Institute of Clinical Studies (NICS) to help develop national guidelines for Prevention of Venous Thromboembolism.

The Division is also contributing to national 'guidelines for guidelines' such as designing new national standards for determining levels of evidence and grading recommendations.

Magnesium Sulphate Clinical Practice Guidelines

Caroline Crowther, Philippa Middleton, Tanya Bubner and Helena Oakey formed part of the multidisciplinary panel whose aim was to provide practical evidence-based guidelines on the best practice for clinical care in the use of magnesium sulphate prior to birth for neuroprotection of the neonate. These guidelines will be relevant for health professionals who care for women at risk of preterm birth and their babies, for pregnant

women and families, and for policy makers in maternity care.

An educational meeting aimed at finalising the draft guidelines was hosted by ARCH in December 2009. Following this meeting a draft version of the guidelines was released for public consultation on 19 December 2009. The draft guidelines were launched in March 2010 and are available on the ARCH website: **www.adelaide.edu.au/arch**

RESEARCH NETWORKS AND EDUCATION

Research Leaders: Professor Caroline Crowther, Professor Jodie Dodd, Ms Philippa Middleton, E/Professor Jeffrey Robinson

The Research Networks and Education Division aims to provide high profile research opportunities by identifying research gaps and defining research questions of major importance in maternal and perinatal health.

Through the Cochrane Collaboration, researchers within ARCH continue to provide:

- Educational training workshops, Cochrane work-ins, and a mentoring program for individual review authors, as well as encouraging maternal and perinatal health professionals to become authors of systematic reviews
- A high-profile program of research training and support in maternal and perinatal health for students, early career researchers and health professionals, including the program with RANZCOG coordinated by Jodie Dodd and Rosalie Grivell.

Further funding was received from the NHMRC to continue the WOMBAT Collaboration (WOMen and Babies' Health and Wellbeing: Action Through Trials). Through the WOMBAT Collaboration ARCH continues to:

- Provide national and regional support for the design, initiation, recruitment, completion, publication and dissemination of results of perinatal clinical trials
- Provide high quality, multidisciplinary education and training in the management of clinical trials
- Facilitate high profile research opportunities by identification and dissemination of research questions needing trials arising from systematic reviews
- Identify further opportunities to form or join research networks (international and national) in maternal and perinatal health.

During 2009 ARCH, through the WOMBAT Collaboration, held a number of training workshops and produced a WOMBAT Trials Booklet (Australian randomised trials in maternal and perinatal health) and a WOMBAT Research Gaps handout (maternal and perinatal research gaps identified from Cochrane reviews) (www.wombatcollaboration.net).

AWARD & FELLOWSHIP HIGHLIGHTS

Professor Alastair MacLennan

South Australian Science Excellence Award - Excellence in Research for Public Good 2009

Dr Alice Rumbold

South Australia Science Excellence Award– South Australian Young Tall Poppy 2009

Discipline of Obstetrics and Gynaecology Award – Most Outstanding Early Career Researcher 2009

Dr Rosalie Grivell

PSANZ New Investigator Award – "Fetal adiposity measures in obese and overweight pregnant women -interobserver agreement" (RM Grivell, H Oakey, N Parange, JM Dodd) – 2009

RANZCOG ASM John O'Loughlin Medal – "Caesarean Section Wound Infection" - 2009

RANZCOG ASM Bayer Schering Prize - "Caesarean Section Wound Infection" – 2009

RANZCOG Fotheringham Fellowship – "Skin and Subcutaneous Fascia Closure at Caesarean Section: A randomised controlled trial" - 2008-2010

Ms Joanna Tieu

PSANZ New Investigator Award "Screening for gestational diabetes mellitus for improving maternal and infant health" (J Tieu, PF Middleton, AJ McPhee, CA Crowther) – 2008-2009

Ms Jessica Broadbent

Discipline of Obstetrics and Gynaecology Award – Head of Discipline Award – 2009

Dr Jodie Dodd

NHMRC Practitioner Fellowship – 2010-2014

NHMRC Neil Hamilton Fairley Postdoctoral Fellowship "Preterm birth: trials and tribulations." - 2006-2009

THE FUTURE

ARCH through its 2008-2012 Strategic Plan has a core commitment to research, education and training to ensure that high quality and timely maternal and perinatal research is conducted, evaluated and translated into health policy and clinical practice. The Plan is aligned with those of the University of Adelaide and research will continue to focus on programs leading to beneficial advances in health and wellbeing for women and babies worldwide.

ARCH will continue to encourage research training to build research capacity for the future and expand its wide collaborative links with maternal and perinatal health professionals within Australia and internationally for research collaboration and implementation.

ARCH has an enthusiastic team of experienced leaders, dedicated multi-disciplinary staff, emerging research fellows and great students to fulfil its vision to improve the health and wellbeing of women and babies worldwide.

Robinson ORIGINS OF HEALTH Institute

THE UNIVERSITY OF ADELAIDE AUSTRALIA

SUB CRUCE LUMEN

RESEARCH CENTRE FOR EARLY ORIGINS OF HEALTH AND DISEASE

Centre Directors' Report

The Research Centre for Early Origins of Health and Disease (EOHaD) is engaged in the investigation of the intergenerational and perinatal origins of metabolic, respiratory, neurological and reproductive health in postnatal life, particularly as we age.

Major activities in 2009 revolved around defining how the early environment before and after birth affects development and health in childhood and later life, specifically including:

- the role of maternal nutrition in affecting respiratory health and allergic disease, including asthma in children
- the impact of prematurity on motor control, cognition and other neurological functions in childhood and older age, and development of novel therapies to rehabilitate impaired motor function after poor early development or in brain injury
- maternal and fetal treatments with growth promoting peptides, including growth hormone, to improve placental function and fetal growth and survival.

Targeted Research Areas

- Intergenerational growth and risk of metabolic disorders
- Early life influences on obesity and fat patterning in children: critical periods, environmental determinants and socio-cultural context
- Perinatal origins of neuromotor and cognitive dysfunction
- Human neuromotor plasticity, ageing and repair
- Maternal stress and sex differences in perinatal growth and survival: maternal asthma, fetal growth restriction
- Early life programming of diabetes and obesity by fetal growth restriction, maternal obesity
- Functional and epigenetic consequences of maternal micro and macronutrient deficiencies or supplementation for metabolic and neurological function of offspring

Centre Directors

Professor Julie Owens

Associate Professor Michael Davies

Associate Professor Michael Ridding

RESEARCH GROUPS

Early Origins of Health and Disease Research

Research Leaders: Professor Jeffrey Robinson and Professor Julie Owens

The Early Origins of Health and Disease group focuses on those aspects of health that are profoundly influenced by events in early life and possibly in previous generations, including diabetes, obesity and cancer risk.

The group aims to understand how common exposures in early life affect our later health and the mechanisms involved (including how these early life exposures interact with the genome and affect the epigenome to determine our later health), and to identify interventions to either prevent the conditions that initiate programming of our later health or to overcome or reverse such programming.

Research Priorities:

- Early life programming of diabetes and obesity–fetal growth restriction, maternal obesity
- Functional and epigenetic consequences of maternal micro and macronutrient deficiencies for metabolic function and cancer risk of offspring
- Micronutrient, dietary and other interventions in mother and offspring to overcome placental programming of metabolic disease
- Efficacy of micronutrient and other interventions in mother and offspring and their molecular and epigenetic basis.

Life Course and Intergenerational Health (LIGHt)

Research Leaders: Associate Professor Michael Davies and Associate Professor Vivienne Moore

The Life Course and Intergenerational Health (LIGHt) group is an interdisciplinary team that focuses on understanding health and wellbeing across the gendered and reproductive life course.

The overall aim of the group is to identify opportunities for the prevention of serious diseases among women and their children, focusing on the social and biological pathways to health at different points in the life course.

This research considers life course and intergenerational issues from a bio-cultural perspective, using a broad range of theoretical and methodological insights to understand the complexities of health. Our goal is to produce innovative research, inform and influence policy, and to build capacity for social change. Our expertise encompasses epidemiology, biostatistics, anthropology, sociology, women's health, reproductive health, and ageing.

The research program is underpinned by three established community-based cohort studies – the Assisted Reproductive Technologies birth cohort, the Lucina cohort, and the Generation 1 cohort. Broadly speaking, these studies are examining the risk and sources of birth defects in children and cancer in women following infertility treatment; the social and biological origins of reproductive problems in women, and the role of early life factors for the optimal development and life-long health of children. A related strand of research is concerned with the implications of gender roles and gender relations for the health of women and their children.

Research Priorities:

- Safety and effectiveness of Assisted Reproductive Technologies (ART)
- How the reproductive health of women can be optimised
- Early life experiences and health outcomes in children
- How gender relations and other socially embedded conditions affect the health of women and children

Neuromotor Plasticity and Development (NeuroPAD)

Research Leaders: Associate Professor Michael Ridding and Dr Julia Pitcher

The Neuromotor Plasticity and Development (NeuroPAD) group researches the way that the brain, nerves and muscles create and control movement in the human body.

There are two major aims of the research. Firstly, the group is interested in how the early environment (both during pregnancy and after birth) influences development of the motor areas of the brain, and how this affects neurologic function, learning and memory during childhood and older age. The second major aim is to develop new treatments that will rehabilitate impaired motor function in those suffering from brain injuries or altered brain development, such as stroke victims and preterm children.

There is emerging evidence that the motor regions of the brain contribute to much more than movement. For example, the group recently found that under-development of the motor areas of the brain due to preterm birth appears to have a negative influence on the development of cognitive abilities, particularly those related to language comprehension, speech perception and working memory in children aged 11-12 years. Therefore, the work of NeuroPAD has already begun to extend to cognitive as well as motor development and function.

Importantly, our research in this area draws on the notion of neuroplasticity, a field pioneered by British physiologist Sir Charles Sherrington (1857–1952). He was one of the first to show that the motor cortex in the brain is not "hard-wired", but "plastic" and adaptable to change. We now know that neurons in the brain reorganise themselves according to new experiences, and that the act of thinking, acquiring new information, and undertaking physical tasks can alter the brain's structure and functions.

We are building on this knowledge to unravel the links between motor skills (controlled movement) and cognitive development (comprehension) in order to reverse motor abnormalities, and improve the quality of life of those suffering from motor dysfunction.

Research Priorities:

- Characterise the impact of preterm birth and/or low birth weight on neurophysiologic development of the motor system
- Characterise the impact of preterm birth and/or low birth weight on the development of motor skills and cognitive abilities
- Characterise the impact of preterm birth and/or low birth weight on neuromotor plasticity

CASE STUDY

RESEARCH NAMED AMONG NATION'S BEST

Research from the Research Centre for Early Origins of Health and Disease is linking cognitive outcomes in children born pre-term with impaired motor development. This research was named among the top 10 health and medical research projects in Australia in 2009 by the National Health and Medical Research Council (NHMRC).

Led by Dr Julia Pitcher, the research discovered that babies born before the optimal gestation period of 40 weeks or below their predicted birth weight show reduced motor system development, which can affect them much longer than previously thought.

Underdevelopment of these motor areas appears to have a negative influence on cognitive abilities related to language comprehension and reading. This is the first physiological evidence that motor and cognitive dysfunction commonly experienced by preterm children when they reach school age probably has common underlying origins in the brain. One of the main impacts of the team's research relates to these late or mildly pre-term children, born between 33 and 37 weeks of gestation. Many of the babies present as normal at birth, but there is increasing evidence that the children experience significant motor, cognitive and behavioural difficulties at school age.

Every week of gestation is important in ensuring normal brain development, so apart from early identification of at-risk infants and development of new therapies, the findings raise some questions about when we induce births. The good news is that it appears a stimulating postnatal environment can ameliorate many of the negative consequences of pre-term birth on both motor and cognitive development.

The long-term aim of the work is to develop early diagnostic and intervention strategies to minimise the impact of preterm birth and enable these children to realise their full potential at school and into later life.

Below: Dr Julia Pitcher and Associate Professor Michael Ridding, Research Leaders Neuromotor Plasticity and Development

Named among the top 10 health and medical research projects in Australia in 2009

- Examine genetic influences on neuromotor development
- Develop effective experimental techniques for inducing functionally beneficial plasticity
- Characterise the impact of general anaesthesia on the motor systems of children

Pregnancy and Development

Research Leader: Associate Professor Vicki Clifton

The Pregnancy and Development group focuses on the mechanisms that contribute to the growth of the fetus in human pregnancy and how problematic events during pregnancy alter those mechanisms to predispose the infant to diseases later in life. The group is particularly interested in pregnancies complicated by asthma and pregnancies complicated by preterm delivery.

Research also examines why male and female babies respond differently to a stress during pregnancy, with the female being more likely to survive and the male being more likely to be associated with poor growth, preterm delivery or death.

Research Priorities:

- Effect of asthma during pregnancy on maternal health, placental function and fetal growth
- Genetic alterations in placental function that contribute to the development of allergy in children
- Programming of the preterm neonatal immune system
- Impact of oxidative stress on preterm neonatal survival
- The role of iodine supplementation on cognition in primary school age children
- The impact of nurse-led antenatal care on maternal asthma severity during pregnancy
- The role of new media in health education of pregnant women.

AWARD & FELLOWSHIP HIGHLIGHTS

Dr Alice Rumbold

2009 South Australian Young Tall Poppy of the Year Award

Dr Lynne Giles

Centre for Intergenerational Health Early to Mid Career Postdoctoral Research Fellowship

Dr Nicolette Hodyl

Colin Matthews Research Award

Dr Melissa Whitrow

Early Career Award for best oral presentation by an early career research fellow at the 'Epidemiology over the Lifespan' meeting of the South Australian Chapter of the Australasian Epidemiological Association

Dr Julia Pitcher

MS McLeod Research Fellowship in Paediatric Medicine, MS McLeod Trust and Women's & Children's Hospital Research Foundation

10 of the Best Research Projects 2009, by the Australian National Health and Medical Research Council

Associate Professor Vivienne Moore

South Australian Women's Honour Roll

THE FUTURE

The Research Centre for Early Origins of Health and Disease will maintain a multi-disciplinary research approach into the future to ensure our research focuses on the issues most relevant to human health.

The Centre will continue to assist in the translation of research outcomes into guidelines and interventions for early life to promote health.

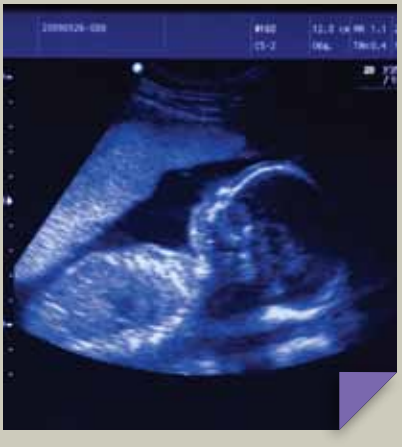
Research priorities for the centre include:

- Defining genetic factors that interact with the early life environment to influence metabolic, respiratory, neurological and reproductive health in postnatal life, particularly as we age
- Identifying epigenetic pathways in early life programming of later metabolic and neurological health
- Demonstrating early life programming of risk of cancer, including prostate cancer, and the underlying pathways

The Research Centre for Early Origins of Health and Disease is also looking to expand on core facilities to include non-invasive body composition analysis of infants and adults and cutting edge MRI facilities.

CASE STUDY

SEX OF BABY DRIVES RESPONSE TO PREGNANCY STRESS



Research is showing that a baby's sex determines the way it responds to stressors during pregnancy and its ability to survive pregnancy complications. Male and female babies during pregnancy show different growth and development patterns following stressors such as disease, cigarette use or psychological stress during pregnancy.

The research is being carried out by the Pregnancy and Development Group, based at the Lyell McEwin Hospital and led by Associate Professor Vicki Clifton. The research has found that male and female babies will respond to a stress during pregnancy by adjusting their growth patterns differently.

The male, when mum is stressed, pretends it's not happening and keeps growing, so he can be as big as he possibly can be. The female, in response to mum's stress, will reduce her growth rate a little bit; not so much that she becomes growth restricted, but just dropping a bit below average.

When there is another complication in the pregnancy - either a different stress or the same one again - the female will continue to grow on that same pathway and do okay but the male baby doesn't do so well and is at greater risk of pre-term delivery, stopping growing or dying in the uterus.

Vicki says this sex-specific growth response had been observed in pregnancies complicated by asthma, preeclampsia and cigarette use but was also likely to occur in other stressful events during pregnancy such as psychological stress. This sex-specific growth pattern was a result of changes in placental function caused by the stress hormone cortisol.

In female babies, increased cortisol produces changes to the placental function which lead to the reduction in growth, but the increased cortisol levels in a mother carrying a male baby don't produce the same changes in placental function.

This research could lead to sex-specific therapies in pre-term pregnancies and premature newborns. It is important in helping obstetricians more accurately interpret growth and development of the fetus in at-risk pregnancies.

The research looks at what events during pregnancy cause changes in how the baby grows, what's behind this and ways in which we can improve the outcomes for pregnant women and their babies.

Robinson Institute
REPRODUCTIVE HEALTH

THE UNIVERSITY OF ADELAIDE
AUSTRALIA
SUB CRUCE LUMEN

RESEARCH CENTRE FOR REPRODUCTIVE HEALTH

Centre Directors' Report

During 2009 the Research Centre for Reproductive Health (RCRH) focused on consolidating and expanding our activities to foster excellence in reproductive biology and medicine research, while also maintaining our significant role in the development of the Robinson Institute.

Major achievements over the year were the successful investment of financial and people resources in developing bids for NHMRC and other equipment funding schemes. We achieved 100% success in four applications for state-of-the-art cell biology and imaging equipment valued at more than $250,000. Complementing the AIB Labs Epigenetics facility funded by BioInnovation SA, and with the Robinson Institute's financial investment, we began to establish a Gene Silencing and Expression (GSEx) facility. Such developments are driven by our strategy to provide core facilities and invest in platform technologies that will expand our research capability and facilitate first-rate research outcomes by RCRH members and the Institute's other Centres. Developing the technical skills and experience of our members through interstate laboratory visits and workshops is a related initiative we want to develop in the future.

A major ongoing activity is to convene regular meetings between Research Program Leaders to discuss new areas of research and opportunities for collaboration and growth. We look forward to exploring new ways to promote communication and interaction between groups and we encourage our early and mid-career scientists to play an important role in this.

The RCRH puts a high priority on providing opportunities for our young researchers to communicate their research at national and international conferences and in 2009 we were able to support travel of more than 20 students and postdoctoral fellows to key meetings where many received awards for best oral and poster presentations. We also provided financial sponsorship for conferences convened by our members, including the International Federation of Placental Associations (Adelaide, October 2009) where research from several RCRH groups was showcased.

There were several notable achievements in 2009 with special congratulations to Dr Darryl Russell for his ARC Future Fellowship and to Associate Professor Claire Roberts for the International Federation of Placental Associations Award in Placentology. Other highlights were the Society for Reproductive Biology RCRH Award for excellence in reproductive biology research to Dr Rob Gilchrist, SRB New Investigator Award to Ms Alison Care, and SA Government Awards to Professor Rob Norman and Professor Alastair MacLennan.

Centre Directors

Professor Sarah A Robertson

Associate Professor Jeremy G Thompson

RESEARCH GROUPS

Circadian Physiology

Research Leader:
Associate Professor David Kennaway

More than 17% of the Australian workforce is engaged in shift-work and the work schedules that these workers are subjected to disrupts hormonal and sleep rhythms, eating patterns and light exposure. Epidemiological evidence is emerging that shift-work increases the risks of developing metabolic syndrome (obesity, insulin resistance and cardiovascular disease), certain cancers (e.g. breast cancer) and infertility. The physiological mechanisms that must underpin these problems are poorly understood, but the recent discoveries of rhythmic gene expression in specialised cells in the brain and every other cell in the body has led to the prediction that disruption of cellular rhythms in the liver, muscles, adipose, brain and the reproductive system will have important health consequences.

The Circadian Physiology group uses state-of-the art molecular biological and physiological approaches and animal models to increase our understanding of how the type of rhythm disruption that shift-workers are subjected to adversely affects their health. Our projects address the role of rhythmicity and the impact of disrupted rhythmicity in reproduction, metabolism and behaviour.

Research Priorities:

- The role of clock genes in reproduction
- Seasonal reproduction in pigs
- The role of clock genes in the maintenance of metabolic homeostasis
- The effects of antidepressant drugs on neurotransmitter receptor gene expression in the brain

Comparative Biology of Mammalian Sperm and Eggs

Research Leader: Associate Professor Bill Breed

The Comparative Biology of Mammalian Sperm and Eggs group is interested in the diversity of life, its evolution and its conservation. As comparative mammalian reproductive biologists the group's main focus is on a study of the evolution of sperm and oocytes (eggs) together with the molecular and cellular processes that take place at the time of fertilisation.

Recently the group investigated the molecules involved in the sperm binding to the oocyte coat glycoprotein, the zona pellucida, and we have found evidence for some differences between closely related species, suggesting the occurrence of positive selection acting on these molecules.

The group also studies the effects of high body temperature on sperm function (with a view to making predictions as to possible male fertility effects of global warming) and we have found that in house mice, and even in arid zone adapted native Australian rodents, there is an increased incidence of apoptosis in sperm residing in the epididymis when animals are exposed to environmental temperatures just a few degrees higher than that of core body temperature.

Research Priorities:

- Coevolution of male and female gametes and reproductive tracts in rodents
- Selective pressures on oocyte coat receptors for sperm binding proteins
- High body temperature effects on sperm quality
- Structural and functional significance of interspecific differences in acrosomal morphology
- Evolution of sperm head cytoskeleton and its functional significance
- Effect of population size on reproductive fitness in marsupials with species reference to wombats

Early Development

Research Leader:
Associate Professor Jeremy Thompson

The Early Development group studies the metabolic and cell signalling involved in the earliest events of mammalian development. Specifically, the group is interested in how oocytes mature and how early embryos grow, and what the impact of the environment that surrounds oocytes and embryos has on their growth, both in the short and long term.

This is important as we now realise that change in the "micro-environment" during the time oocytes mature and embryos are formed can have effects on not only early development, but on fetal and placental development and even health of the child and potentially the adult. This is particularly concerning considering that 3% of Australian babies are created using IVF techniques, which is an "artificial" environment

Targeted Research Areas

- Ovarian and follicular function
- Oocyte and early embryo development
- Uterine biology
- Embryo implantation and placental development
- Male reproduction
- Reproductive immunology
- Human and Animal Reproductive Biotechnology
- Nutrition, environment and reproduction
- Health and social outcomes in reproduction
- Early life programming of fetal development and adult health
- Menopause
- Infectious diseases of the reproductive and gestational tissues
- Contraception
- Cancers of the reproductive system

that provides sufficient support for early development to proceed, yet may leave an unmeasured legacy later in life.

This work focuses on the role of oxygen concentration and associated signalling mechanisms, energy substrate utilisation and metabolism and cellular signalling in response to metabolism and, finally, how peptide hormones produced by the reproductive tract affect metabolic and developmental profiles.

The group has been active in developing commercial products for the assisted reproductive technology industry, in both clinical and agricultural applications. Specifically, developing nutritive solutions for human oocytes and embryos (and for other species), which are then manufactured and marketed by companies.

Our research has shown that the metabolic environment surrounding oocytes during the first hour of in vitro maturation is critical to subsequent oocyte developmental competence. This is relevant to practice, as many operators aspirate oocytes with simple buffered solutions. The group has also developed new media systems for human in vitro maturation that significantly support maturation, which are currently under clinical trial evaluation.

Research Priorities:

- Oocyte maturation
- Metabolic signalling and regulating oocyte competence
- Role of oocyte secreted factor regulating oocyte competence
- Role of oxygen and Hypoxia Inducible Factor in Reproductive Biology
- Role in oocyte maturation and ovarian function, early embryo development and placental development and function
- Production of clinical and veterinary products for more efficient delivery of reproductive technologies

JS Davies Epigenetics and Genetics

Research Leader: Professor Stefan Hiendleder

The JS Davies Epigenetics and Genetics group is focused on understanding how epigenetics impacts on pre- and postnatal development and health.

Epigenetic programming of DNA via epigenetic modification such as DNA methylation is responsible for epigenetic effects on gene expression and phenotype. Prenatal environmental cues can trigger epigenetic change with lifelong effects on health and disease. The group has a special interest in determining the effect of genetic differences on epigenetic programming and phenotype.

In 2009 the group discovered an unexpected high variation in DNA methylation levels in somatic cell nuclear transfer animals and that epigenetic plasticity is dependent on maternal genetics in a bovine model system.

Research Priorities:

- Role of epigenetic mechanisms in embryonic and fetal development
- Sex chromosome effects
- Novel non-mendelian modes of inheritance

Gamete and Embryo Biology

Research Leader: Dr Michelle Lane

The Gamete and Embryo Biology group is focused on understanding how oocytes, sperm and embryos develop and what the impact of the environment is to their health.

The group has a special interest in exploring the underlying cause of infertility and to develop better treatment strategies to improve the success of human assisted reproductive technologies.

Research Priorities:

- Mammalian oocyte biology
- Mammalian preimplantation development
- Sperm biology
- IVF/assisted reproduction
- Obesity and infertility

Menopause Research

Research Leader: Professor Alastair MacLennan

The Menopause Research group is a multidisciplinary group based in the Discipline of Obstetrics and Gynaecology at the Women's & Children's Hospital. It conducts epidemiological studies, large clinical trials and educational programs on the menopause and postmenopausal women's health.

The group played a major educational role in 2009 by supporting frequent clinical and scientific evening meetings with the Adelaide Women's Health Group. The group also contributed to the results of LIBERATE, a randomised placebo control trial of tibolone after breast cancer. The group's epidemiological research continues using the South Australian Health Omnibus Survey and currently the group is participating in a multicentre clinical trial of a new hormonal contraceptive skin patch, which will continue until 2011.

Research Priorities:

- Epidemiological studies on pelvic floor dysfunction, alternative therapies and hormone therapy use, quality of life in collaboration with the Department of Health. Population Research and Outcome Studies Unit using the SA Health Omnibus Survey.
- Cochrane collaboration systematic review on HRT and vasomotor symptoms.
- The Women's International Study of Long Duration Oestrogen after Menopause (WISDOM).
- Research into Memory, Brain function and Oestrogen Replacement (REMEMBER study) and genetic sub study.
- Tibolone after breast cancer four-year study (LIBERATE).
- Long-term Intervention on Fractures with Tibolone Trial (LIFT).
- Phase I, II and III studies on new treatments for menopause and osteoporosis.

Molecular Reproduction

Research Leader: Professor Richard Ivell

The Molecular Reproduction group is focused on the molecular biology of differentiation processes in both the male reproductive system and in female reproduction. The group is especially interested in how xenobiotic compounds from the environment impact upon the development of the reproductive system of the embryo during pregnancy and early perinatal life, and its later effect in ageing.

There is a special focus on the development of the male reproductive system and the factors responsible for correct testis formation and the descent of the testes into the scrotum at birth. An important aspect of the groups work looks at the family of relaxin-like peptide hormones and their role in gender determination and health in both men and women. In particular we have shown that insulin-like peptide 3 (INSL3) is an essential component in the establishment of male gender, and appears to be significantly modulated both by xenobiotic action during pregnancy and by preeclampsia.

A further key research interest of the group is to understand the diverse ways that steroid hormones can act within cells to achieve their effects in terms of altered gene expression. This work is of great relevance in understanding how steroid hormones and also environmental xenobiotics can influence the growth of reproductive-related cancers. Of particular interest here are the so-called non-classical mechanisms of steroid action for both estrogenic and androgenic

compounds, which do not appear to involve a direct action of steroid receptors with the control regions of genes. Rather they involve a variety of indirect mechanisms of action within cells and tissues and probably comprise more than 90% of steroid-dependent effects.

A highlight for the group was the first elaboration of the dynamics of INSL3 production and secretion within the male reproductive system for any species.

Research Priorities:

- Role and functioning of relaxin and related insulin-like peptides in human health and disease
- Mechanism of action of environmental xenobiotics during pregnancy and early life, and their impact on reproductive processes, including ageing
- Non-classical pathways used by estrogens and androgens in regulating cell function

Oocyte Biology

Research Leader: Dr Robert Gilchrist

The Oocyte Biology group is interested in ovarian biology and the regulation of mammalian oocyte development, the development of oocyte maturation techniques, and particularly oocyte-somatic cell paracrine signalling.

The research program of the group spans basic discovery research through to applied research and clinical trials. A key objective of the discovery research program is to understand the dynamic cellular signalling between the oocyte and somatic cells of the ovary, and the significance of this signalling on the quality of the oocyte and resultant embryo and fetus. This work has significance for the one in six couples faced with an infertility diagnosis - up to 40% due to female factors - especially those in which ovarian stimulation protocols fail or cannot be performed (such as PCOS cases).

The group works primarily in animal models but is also actively engaged in pre-clinical trials and commercial translation of research to develop new treatments for female infertility.

In 2009, Firas Albuz successfully developed a new approach to oocyte in vitro maturation (IVM) named Simulated Physiological Oocyte Maturation (SPOM) and submitted his PhD on the subject. A provisional patent was lodged on the procedure and human pre-clinical trials commenced at the Free University of Brussels (VUB) in collaboration with Professor Johan Smitz.

"IVF Vet Solutions" was founded as a University of Adelaide business unit by Dr Robert Gilchrist and Associate Professor Jeremy Thompson. They were awarded Commercial Accelerator Scheme funding from Adelaide Research & Innovation and a Commercial Development Grant from the Faculty of Health Sciences.

Research Priorities:

- To adapt and validate our new approach to oocyte in vitro maturation (IVM), Simulated Physiological Oocyte Maturation (SPOM), to mouse oocytes and human oocytes
- To characterise the interactions in cumulus cells between intracellular GDF9 and EGF signalling
- To generate new GDF9/BMP15 constructs, cell lines and purified recombinant proteins
- To adapt and validate the SPOM system to veterinary field conditions

Ovarian Cell Biology

Research Leaders: Professor Robert Norman, Dr Rebecca Robker and Dr Darryl Russell

The Ovarian Cell Biology group is a collaborative research team elucidating hormonal, nutritional and intra-ovarian regulatory mechanisms governing ovarian functions; specifically the release of mature fertilisation competent oocytes and the production of steroid hormones.

Within the ovary, specific cell types are arranged into follicle structures with unique and highly specialised functions. These cells coordinate a growth-promoting microenvironment in which oocytes undergo an intricate progressive developmental process. Follicle cells integrate maternal cues to direct the growth and timely release of the oocyte, and determine its capacity to form an embryo.

The research aims of the group are to understand how distinct maternal signals establish and modulate this niche environment, and how it dictates the differentiation and successful release (ovulation) of oocytes. The research focuses broadly on cellular mechanisms that control these ovarian functions, including hormone action, regulation of transcription, intercellular communication, cell-matrix interactions, cellular migration and proteolytic tissue remodelling.

Overall, the group's work is revealing basic molecular processes critical for reproductive success and elucidating maternal hormone, immunological and metabolic inputs through which modern lifestyle and environment impact on the health of the oocyte and hence a healthy start to life.

In 2009 the group found that the ovarian follicular environment of obese women is dramatically different than that of moderate weight women; specifically there were high levels of insulin, glucose and particularly lipids in the ovarian fluid surrounding the oocytes of obese women.

The group also found that the ovarian lymphatic system develops postnatally under the regulation of lymphangiogenic growth factors and proteolytic enzymes. Further research of the group has resulted in very novel findings that the cells of the cumulus oocyte complex adopt a migratory phenotype at the time of ovulation.

Research Priorities:

- Identifying molecular mechanisms that control ovulation
- Identifying biomarkers of oocyte developmental competence
- Understanding regulation of lipid metabolism in the cumulus-oocyte-complex
- Determining why maternal obesity and Polycystic Ovary Syndrome (PCOS) impair ovulation and diminish oocyte developmental competence
- Molecular control of ovarian primordial follicle activation
- Investigating how immune cells influence ovarian function
- Elucidating development and function of the ovarian lymphatic system

Ovarian Developmental Biology

Research Leader: Professor Ray Rodgers

The Ovarian Developmental Biology group aims to discover key aspects of ovarian development that underpin our understanding of infertility and endocrine diseases involving the ovary, and to develop prevention and treatment strategies for these.

The group focuses on the roles of extracellular matrix. Matrix is diverse and complex and regulates many cellular and tissue functions. It has been largely overlooked in comparison with the numerous studies of hormones and growth factors in the ovary and hence holds potential for many new discoveries.

Research Priorities:

- Novel concepts on the aetiology of polycystic ovarian syndrome
- Oocyte quality
- Focimatrix and maturation of follicles
- Formation of follicular fluid

CASE STUDY

GENETIC TEST FOR PREGNANCY RISK CLOSER TO REALITY

Robinson Institute researchers, led by Associate Professor Claire Roberts in the Placental Development Group, are working on developing a world-first genetic test that can predict which pregnancies are at risk of complications long before symptoms arise.

Researchers have identified subtle variations in specific genes within the mother, father or baby that indicate the mother is more likely to suffer from pregnancy complications.

Pregnancy success is determined by a complex interaction of maternal, paternal and environmental characteristics that together dictate how well the placenta develops and functions and how the mother adapts to pregnancy.

Defects in placental development and function are implicated in common pregnancy complications ranging from miscarriage, through preeclampsia, pre-term birth and fetal growth restriction.

The problem with complications is that we are currently unable to predict which women are at risk until symptoms develop, and then therapies can be too little, too late.

This research advancement will permit tailored and potentially life-saving antenatal care and constitutes a significant leap forward in the care of pregnant women and their babies.

The research has also identified potential therapies for use in early pregnancy to improve placental development and function and reduce the risk of pregnancy complication.

The Research Centre for Reproductive Health is part of the international SCOPE (Screening for Obstetric and Pregnancy Endpoints) program. Through the South Australian arm of this study we have recruited almost 1,500 patients and have taken samples from mother, baby and father to build a pregnancy biobank to screen candidate markers of pregnancy disease.

Below: Associate Professor Claire Roberts

Over 1500 patients recruited and samples added to our biobank.

Placental Development

Research Leader:
Associate Professor Claire Roberts

Clinical Leader: Professor Gus Dekker

The Placental Development group aims to identify pre-pregnancy and/or early gestation markers that have the ability to predict a couple's risk for the development of adverse pregnancy outcomes.

The group has identified factors that promote placental development and function and maternal adaptation to pregnancy that interact in determining pregnancy success. The group is part of the international SCOPE consortium, which is a multicentre trial that has currently recruited about 7000 couples around the world.

In Adelaide we recruited 1380 women to SCOPE, the last of whom delivered their babies in March 2009. In addition, the group has another smaller Adelaide-based clinical study: PAPO, Predicting Adverse Pregnancy Outcomes.

Research Priorities:

- Identify single nucleotide polymorphisms (SNPs) that can be used to predict pregnancy outcome
- Combine SNPs and develop a clinical test to identify couples at risk for pregnancy complications long before symptoms arise. This will enable appropriate antenatal care in both high risk and low risk settings
- Perform cell culture work and elucidate the role of the particular genes of interested in trophoblast proliferation and function in order to understand their role in placentation
- Identify circulating micronutrient factors, thrombophilias, hormones and lipids associated with adverse pregnancy outcome
- Determine if DNA damage in sperm is correlated with DNA damage in peripheral lymphocytes
- Determine if B-vitamins and SNPs are associated with DNA damage in either sperm or peripheral lymphocytes
- Determine if DNA damage in mothers and fathers is associated with adverse pregnancy outcome
- Determine that the polymorphisms we have identified have functional effects on gene expression in the placenta
- Provide further proof-of-concept that our new embryo media formulation improves implantation rate, placental development and has no adverse effects on post-natal growth trajectory and reproductive potential of offspring

Reproductive Cancer Research

Research Leaders: Dr Carmela Ricciardelli and Associate Professor Martin Oehler

The Reproductive Cancer Research group has three core research projects:

1. Proteomics of ovarian cancer implantation

The implantation of cancer cells onto the peritoneal surfaces is one of the first crucial steps in ovarian cancer metastasis. It remains unclear which factors promote this process. The group recently investigated the interaction between ovarian cancer cells and peritoneal cells using a proteomic approach. This novel strategy aimed to identify important proteins likely to be mechanistically involved in implantation to the peritoneum, one of the first steps involved in ovarian cancer metastasis.

2. Immunoproteomics approach to identify early detection markers in ovarian cancer

At present there is no reliable biomarker for the diagnosis of early stage ovarian cancer. Since there are no specific symptoms related to ovarian cancer, a large proportion of women with ovarian cancer are diagnosed when they have late-stage disease. Only 35% of women with advanced ovarian cancer are alive after five years following diagnosis. In contrast, the five-year survival for patients diagnosed with the organ-confined stage I ovarian cancer exceeds 90%, and most patients are cured of their disease. Autoantibodies against tumour associated antigens have recently emerged as promising biomarkers for the detection of cancer and may provide an early, useful and effective marker for the detection of ovarian cancer. A project funded by Ovarian Cancer Research Foundation (OCRF) in 2009 investigated the presence of autoantibodies in ovarian cancer patients and their potential as diagnostic markers. Several autoantibodies have been detected in advanced stage serous ovarian cancer patients. Ongoing studies will determine if a panel of these antibodies are also present in early stage ovarian cancer and be used for ovarian cancer diagnosis.

3. Maldi imaging of early ovarian cancer development

The group is also exploring the proteomic profile of early stage serous ovarian carcinomas and tubal intraepithelial carcinomas by means of imaging mass spectrometry (IMS). IMS which applies Matrix-Assisted Laser Disorption Ionisation-Time Of Flight Mass Spectrometry (MALDI-TOF MS) directly on tissue sections for mass measurement of proteins and peptides, has become a powerful, high interest field in proteomics as it allows sampling of numerous individual masses and their distribution in tissue sections. The project will be the first to investigate the proteome in early stage ovarian cancer by means of IMS. Results from this project have the potential to translate into a fundamental new understanding of ovarian cancer.

Reproductive Cancer Cell Biology

Research Leaders: Dr Darryl Russell and Dr Carmela Ricciardelli

The Reproductive Cancer Cell Biology group studies the interaction between cancer cells and their microenvironment that promotes the progression of reproductive organ cancers to invasive and metastatic disease.

About 1/3rd of breast and prostate cancer patients will develop metastatic disease which available therapies cannot cure. Advances in early detection of malignancies have done little to improve the proportion of patients who face early relapse and mortality due to the disease.

This group is investigating the molecular mechanisms that enable these metastatic cancer cells to detach from the primary tumour mass and migrate into blood or lymphatic vessels that give them passage to new sites where metastases establish. To do this cancers acquire the capacity to remodel their surrounding extracellular matrix by making key protease enzymes.

The group has identified specific members of a protease family known as the ADAMTS family, which is associated with poor prognosis for breast and prostate cancers respectively. We are using mouse models of cancer metastasis as well as cell culture systems with engineered over-expression or knock-down of specific genes with specific gene mutations to investigate the influence of proteases on metastatic cellular behaviour.

These exciting results show that members of the ADAMTS family of protease enzymes are produced by aggressive cancer cell types in human disease and in our mouse models. These promote remodelling of the extracellular matrix that normally surrounds cancers, changing the interactions between tumour cells and their neighbouring non-malignant stromal tissue to enhance tumour growth and metastatic spread. This work is revealing potential biomarkers to identify the patients who are at risk of metastatic relapse as well as promising therapeutic targets to block the metastatic process.

Research Priorities:

- Characterising mechanisms by which ADAMTS proteases promote tumour grade and metastatic progression in mouse models

- Determining the association of protease expression with tumour grade and prognosis in human patients
- Identifying protease substrates in tumour associated extracellular matrix
- Understand the consequences of protease-substrate interaction for metastatic behaviour of human cancer cell lines in a range of culture systems
- Identifying effective inhibitors of ADAMTS catalytic activity or their products as potential anti-metastatic therapeutics

Reproductive Immunology

Research Leader: Professor Sarah Robertson

The Reproductive Immunology group is focused on understanding the immunology and cytokine biology of embryo implantation and establishing healthy pregnancy. In the days after conception the mother's immune system must undergo a transformation to allow the embryo to implant and develop, and failure of maternal immune tolerance to occur is a key reason for infertility and miscarriage.

The group's research shows that immune adaptation in the peri-implantation period not only influences a woman's receptivity to pregnancy, but also impacts pregnancy outcome and health of the baby after birth.

This research seeks to define the sequence of events which generate maternal immune tolerance of the conceptus, including the origin and nature of the biological signals which stimulate immune adaptation to pregnancy. The group has discovered a critical role for the male partner's seminal fluid in conditioning the female reproductive tract for pregnancy. A major focus is to define how seminal fluid causes these changes, and whether some couples experience incompatibility in the seminal fluid signalling pathway.

The group's research tackles the 40% of human infertility attributed to compromised uterine receptivity, since defects in the immune response are thought to underpin this condition, as well as later complications of pregnancy including miscarriage, preeclampsia and preterm delivery. In defining new biological functions for seminal fluid this work also sheds light on forms of male infertility not attributable to conventional sperm parameters. We work in animal models and in humans, and are actively engaged in clinical and commercial translation of our research to develop new treatments for female and male infertility and miscarriage.

Research Priorities:

- What is the mechanism through which immune tolerance is established in early pregnancy to allow the semi-allogeneic embryo to implant and develop?
- Why does this process fail in some women, leading to infertility and miscarriage?

Above: Associate Professor Jeremy Thompson and Professor Sarah Robertson

- Do male seminal factors access the uterine cavity after intercourse in women, to influence fertility through promoting endometrial receptivity?
- What is the identity of the male seminal fluid signalling agents, and the mechanism of delivery of male immune-regulatory factors and antigens? What role does sperm RNA deposition into female cells play in this pathway?
- What are the key signals in seminal fluid, or from the conceptus, that drive the maternal T cell response towards Treg-mediated tolerance as opposed to Th17- and Th1-mediated rejection, and does insufficiency in these factors contribute to male infertility?
- What is the mechanism through which immune responses activated in the peri-conceptual environment impact later placental development and fetal growth?
- Do different macrophage and dendritic cell phenotypes and their regulators influence reproductive tissue development and function?
- Does exposure to seminal fluid influence female reproductive health through effects on the immune response to sexually transmitted infection, and/or incidence of endometriosis?

AWARD & FELLOWSHIP HIGHLIGHTS

Dr Darryl Russell
ARC Future Fellowship

Dr Denise Furness, Dr Prabha Andraweera
Australia and New Zealand Placental Research Association

Dr Louise Hull
Government of SA Clinical Fellowship

Associate Professor Claire Roberts
International Federation of Placenta Associations Award in Placentology

Dr Robert Gilchrist
Society for Reproductive Biology/RCRH Award for Excellence in Reproductive Biology Research

Hassan Bakos
Society for Reproductive Biology/Oozoa Student award for best presentation

Alison Care
Society for Reproductive Biology New Investigator Award

Young Investigator Award

Izza Tan
Society for Reproductive Biology Best Poster

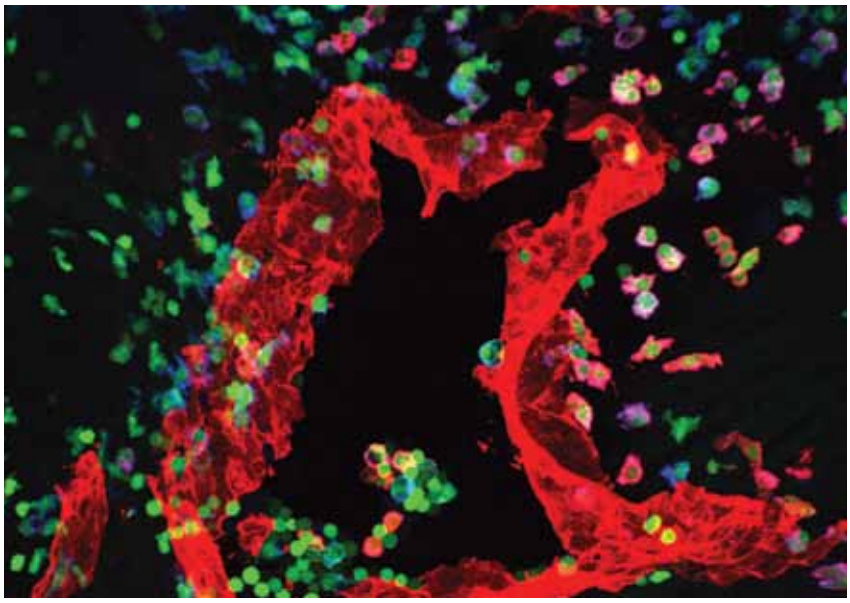
Professor Alastair MacLennan
South Australian Excellence in Research for Public Good Award – Science Excellence Awards

Professor Robert Norman
South Australian Scientist of the Year – Science Excellence Awards

Professor Sarah Robertson
Top 10 Emerging Australian Scientists in the 'Australia's Top 100 Emerging Leaders' feature in the *Weekend Australian Magazine*

Leigh Guerin, Dr Lachlan Moldenhauer, Ang Zhou
YW Loke Award (New Investigators) of the International Federation of Placenta Association

Kathryn Gebhardt
Adelaide Research and Innovation P/L Poster Prize for the best Commercial Research Poster at the Faculty of Health Sciences Postgraduate Research Expo



THE FUTURE

The Research Centre for Reproductive Health will continue to provide first class research infrastructure, equipment and core facilities. A priority for the Research Centre will be to establish the Gene Silencing and Expression (GSEx) Facility. This will provide a key tool in cell biology research that will allow the Centre to maintain its competitiveness as a leader in basic reproductive biology.

The Centre will continue to provide funding opportunities for our researchers through:

- Travel grants to enable PhD students and ECRs:
  - to present their research to peers at international/national conferences
  - to foster future collaborations
  - to provide an opportunity for mentoring and motivation by established leaders in the field.
- Equipment grants
  - Internal/infrastructure grants with support from the School of Paediatrics and Reproductive Health to replace ageing equipment with state-of-the-art technology.
  - Leverage support for NHMRC Equipment grants which will provide distinct, contemporary experimental facilities, promote innovative research and attract and retain leading scientists.

A focus for the Centre will be to support researcher career development. The Centre will provide training for our researchers to update and expand their technical and theoretical knowledge of current core research skills, or for research staff to learn new research skills that can be applied to the targeted themes of the Centre and be of benefit to all members.

CASE STUDY

IMMUNE CELL PREGNANCY LINK A WINNER

In 2009 PhD student Alison Care was named the 2009 winner of the prestigious Young Investigator Award and a $10,000 prize for shedding new light on why some women are infertile and why some pregnancies end in miscarriage. Kathryn Gebhardt, also of the Robinson Institute, was a runner up at the awards.

Alison's research has examined the role of a type of immune cells (white blood cells) known as macrophages within the ovary, which are found in abundance around developing eggs and in hormone-producing structures.

The study, conducted in mice, shows that when these white blood cells are depleted there is a substantial decline in the amount of progesterone the ovary produces. Progesterone is a hormone produced by the ovary that is essential for the maintenance of early pregnancy.

Research shows that the ovary requires a vascular network in order to deliver the high levels of progesterone the body requires to maintain early pregnancy. The formation of this network occurs very quickly following ovulation, and macrophages may be involved in establishing that blood supply.

It appears that the ovary has its own specialist pathway to achieve this, and that macrophages have an essential role in building the blood supply that we hadn't previously appreciated.

This research identifies immune system cells as critical determinants of normal ovarian activity and the maintenance of early pregnancy. This might be a key to helping prevent early pregnancy loss, such as recurrent miscarriage.

A number of factors - such as smoking, obesity, poor nutrition and stress - can alter the way macrophages behave and may provide reasons for infertility or miscarriage in some women and a new explanation for infertility.

Alison Care

Robinson Institute STEM CELLS

THE UNIVERSITY OF ADELAIDE AUSTRALIA

SUB CRUCE LUMEN

CENTRE FOR STEM CELL RESEARCH

Centre Directors' Report

The Centre for Stem Cell Research is an initiative of the University of Adelaide that brings together researchers with a common focus in stem cells at the University, and researchers and affiliate title holders at the Women's and Children's Hospital, SA Pathology, the Royal Adelaide Hospital, The Queen Elizabeth Hospital, and the Hanson Institute.

The Centre consists of over 200 scientists, support staff and postgraduate students, who together attract over $7 million in research funding annually.

During 2009 the Centre continued to implement a number of strategic initiatives based on its Strategic Plan to encourage collaboration among its members and other stem cell researchers, both nationally and internationally. These included networking forums, summer scholarships, collaborative research grants and an annual research forum.

Targeted Research Areas

- Isolation and characterisation of embryonic, adult and iPS cells
- Differentiation of ES cells including nerve, cardiac muscle, cartilage, bone, ligament, pulp, blood, heart, pancreas, kidney, gametes
- Clinical applications: diabetes, stroke, cardiac repair, bone repair, periodontitis, blood disorders, cystic fibrosis and other morbidities conducive to gene and cell therapy

Centre Directors

Associate Professor Mark Nottle

Associate Professor Stan Gronthos

RESEARCH GROUPS

Acute Leukaemia

Research Leader:
Associate Professor Richard D'Andrea

The major focus of the Acute Leukaemia group is to understand the mechanisms underlying normal blood cell growth and differentiation, and the changes associated with initiation and progression of leukaemia. The group is using novel systems to dissect signalling pathways that control cytokine-induced cell survival, proliferation, differentiation and self-renewal.

Aberrant cytokine receptor signalling occurs frequently in acute myeloid leukaemia (AML) and identification of key downstream events will allow development of targeted therapies with reduced toxicity. The group is also utilising molecular and proteomic approaches to identify factors that contribute to the therapeutic response and relapsed disease.

Myeloproliferative disease (MPD) occurs as a result of changes acquired in the haemopoietic stem cell compartment that induce aberrant growth factor responses and over-production of mature myeloid and erythroid cells. Through molecular and genetic cohort studies of patients with MPD we aim to understand the nature of the changes that are associated with disease initiation and long-term maintenance of disease in these patients.

The group is also collaborating with Associate Professor Simon Barry to investigate the mechanisms controlling the regulatory T cell lineage and with Associate Professor Andrew Zannetino to study molecular mechanisms that contribute to bone differentiation.

Research Priorities:

- Increase understanding of the changes that contribute to aberrant blood cell production and disease.
- Develop new approaches to diagnosis and therapy of blood diseases

Blood Cell Growth and Differentiation and the Changes Associated with Leukaemia

Research Leader: Dr Ian Lewis

Umbilical cord blood (CB) is a proven alternative source of haemopoietic stem cells (HSC) for transplantation. The major limiting factor to more widespread use of CB is the characteristic delay in engraftment.

Mesenchymal stem cells (MSCs) are derived from the non-haemopoietic elements of BM and are capable of in vitro differentiation into multiple mesodermal tissue types including osteoblasts, chondrocytes, myocytes and adipocytes. It has been postulated that MSCs may promote HSC engraftment by enhancement of haemopoietic progenitor proliferation, haemopoietic growth factor production or facilitating homing of transplanted cells through adhesion molecules. MSCs have also been shown to be immunosuppressive and thus may promote engraftment by reducing the recipient alloimmune response.

In this project the group has characterised MSCs derived from human placenta and assessed their role in CB transplantation in a non-obese diabetic/severely immuno-deficient (NOD/SCID) mouse model and compared outcomes to transplantation using two umbilical cord blood units.

Acute myeloid leukaemia (AML) is a clonal, neoplastic proliferation of immature myeloid cells of the haemopoietic system, characterised by aberrant or arrested differentiation. Immunological characterisation of leukaemic cells is important in the diagnosis and prognosis of AML and is increasingly being used in the monitoring of the disease. The presence of Minimal Residual Disease (MRD) in the bone marrow (BM) of patients with AML following chemotherapy is strongly associated with relapse of leukaemia. Identification of patients with a high risk of relapse by MRD techniques may enable new therapeutic strategies to be offered to these individuals.

Cardiac Repair

Research Leader: Professor Stephen Worthley

Heart failure resulting from weakened heart muscle remains a major cause of ill health and death in our society, despite improvements in current clinical therapies. Two major types of heart failure exist. Ischaemic heart failure makes up about 60% of cases and is caused by narrowing of coronary arteries, depriving the heart muscle of necessary blood supply.

Non-ischaemic heart failure accounts for the remainder of cases and has various causes including viruses, certain drugs and toxins, and some hereditary and metabolic diseases.

The Cardiac Repair group has researched how different types of stem cells taken from bone marrow have been studied as a way of regenerating and repairing injured cardiac tissue. Mesenchymal stem cells (MSC) are a rare type of cell found in adult bone marrow that have the ability to divide and renew themselves and the potential to develop into different types of mature cells, including bone, cartilage, blood vessel cells and heart cells.

Cystic Fibrosis Gene Therapy

Researcher Leaders: Dr David Parsons and Dr Don Anson

The goal of the Cystic Fibrosis Gene Therapy group is to produce a safe and effective treatment for cystic fibrosis airway disease; ultimately our hope is to produce a cure. To reach this goal the group uses a modified virus to transport the correcting gene directly into the affected airway surfaces, and our unique method is designed to target the adult stem cells that are normally present in the airway cell surface.

When effective, those corrected airway stem cells can automatically generate corrected daughter cells that populate the airway surface. In parallel, the group is also developing new methods using the special X-rays produced by a synchrotron – at facilities in Japan and Melbourne, to improve early detection of the effectiveness of our gene therapy. The group's studies include the use of laboratory mice, and special CF mice, to develop and test these methods to help us translate our findings into realistic therapies for testing in future clinical trials.

Research Priorities:

- Safe and effective airway gene transfer
- Early and non-invasive detection of success or failure of gene transfer in living airways

Gene Technology

Research Leader: Dr Don Anson

The Gene Technology group is focused on the development of lentiviral vector mediated gene therapy for inherited metabolic diseases. The group has developed its own lentiviral vector technology and has considerable expertise in the large scale production and purification of lentiviral vectors.

Diseases of interest are the lysosomal storage disease mucopolysaccharidosis type IIIA, methylmalonic aciduria and cystic fibrosis. Research in these diseases is currently based on the use of animal models to evaluate the efficacy of different approaches to gene delivery. The work is done in collaboration with Dr Sharon Byers (Head, Matrix Biology Lab, SA Pathology) for mucopolysaccharidosis type IIIA, Dr David Parsons (Pulmonary Medicine, Women's and Children's Hospital) and Dr Janice Fletcher, Dr Heidi Peters (Women's and Children's Hospital and The Murdoch Institute, respectively).

Research Priorities:

- Evaluation of lentiviral mediated gene therapy for inherited diseases using mouse models of human disease, namely:
  - Mucopolysaccharidosis type IIIA
  - Methylmalonic aciduria
  - Cystic fibrosis

Mesenchymal Stem Cell Group

Research Leader:
Associate Professor Stan Gronthos

Adult bone marrow contains a non-haematopoietic, stromal stem cell population with the ability to form clonogenic, adherent colonies comprised of fibroblast-like cells (CFU-F: colony forming units-fibroblast). The ex vivo expanded progeny of CFU-F have been shown to develop into different stromal cell lineages (myelosupportive stroma, adipocytes, smooth muscle cells, myoblasts, chondrocytes and osteoblasts) and are thought to arise from a common, self-replicating multi-potential stem cell referred to as mesenchymal stem cells (MSC) or bone marrow stromal stem cells.

The group's stem cell isolation technology has recently been used to identify MSC-like cells from adipose tissue and dental tissues that exhibit similar growth properties and gene expression profiles to these described for bone marrow derived MSC. This work has resulted in the generation of several patents encompassing the isolation and expansion technologies and use of different MSC preparations for various tissue engineering based applications. These patents have now been licensed to two sister companies, Angioblast Systems Inc., New York, NY. and Mesoblast Ltd., Melbourne Vic.

Research Priorities:

- Identify factors and signalling pathways that mediate MSC self-renewal, niche maintenance, proliferation recruitment/migration and multi-differentiation
- Determine the safety and efficacy of MSC-like populations to regenerate functional tissues when implanted into animal models of tissue damage

Mesenchymal Stem Cell Therapy and Gene Therapy in Organ Transplantation

Research Leader: Dr Ravi Krishnan

The focus of this laboratory is on the molecular and cellular mechanisms of rejection of transplanted organs and the development of novel gene and cellular therapy approaches to treat rejection in organ transplantation.

Dendritic cells:

The dendritic cell from the donor organ is the major cell that initiates the rejection response by providing activation signals to the responding T cells from the recipient. The activation signals are provided by costimulatory molecules on dendritic cells, which interact with their appropriate ligands/receptors on T cells. The blockade of signals between these cells produce T cell unresponsiveness that facilitates organ transplant acceptance. Our studies involve the genetic modification of dendritic cells using adenoviral gene therapy vectors to deliver immunomodulatory molecules that belong to the immunoglobulin-like supergene family and the TNF-receptor-like supergene family members. Upon expression of these negative regulatory molecules in dendritic cells the effects on rejection responses and organ transplant acceptance will be studied in experimental models of transplantation.

Mesenchymal stem cells:

Adult mesenchymal stem cells are cells derived from bone marrow that can facilitate tissue repair of damaged or diseased tissue. Furthermore, these cells have the distinct property of differentiating into bone, cartilage and adipose tissues, and intriguingly under appropriate culture conditions can transdifferentiate into insulin producing cells. Pancreatic islet transplantation is currently a clinical treatment for insulin replacement therapy in type 1 diabetics, however, the shortage of donor pancreases is a limitation of this important treatment. Thus MSCs offer an expandable and readily available source of insulin producing cells.

Research Priorities:

- Characterise the immunomodulatory and regenerative properties of adult mesenchymal stem cells for the treatment of transplant rejection and the treatment of diabetes using cellular, molecular and gene therapy strategies
- Evaluate the efficacy of cell therapy (mesenchymal stem cells and dendritic cells) in the treatment of organ transplant rejection and to assess the translational potential in preclinical experimental models

Molecular Immunology

Research Leader:
Associate Professor Simon Barry

The Molecular Immunology group is interested in how a healthy immune system balances being ready to react by swiftly fighting off pathogens, while maintaining tolerance to harmless challenges such as food and body tissues. The cellular immune repertoire in humans is broad, but we are focused on a T cell subset that is shaped, along with the immune system, from birth. These cells are known as regulatory T cells, and they are accepted as the police of the immune system.

There is increasing evidence that in a wide number of disease states including autoimmune diseases such as type 1 diabetes and multiple sclerosis, these cells fail to regulate the immune system, and allow inappropriate destruction of tissues that are essential for life. In order to understand how this breaks down in disease, one must first understand what the basis of a healthy Treg is.

To do this the group is focused on human cells. It uses a number of state-of-the-art gene discovery tools such as microarrays to identify and then confirm the key genes in Treg function. The group has developed a number of lentiviral tools to confirm the functional importance of these genes and these can be applied in any human cell systems. As Treg play a role in autoimmune disease, cancer and transplantation tolerance, our research findings have a wide clinical application.

Research Priorities:

- Identifying the genes responsible for normal regulatory T cell function using genome-wide approaches
- Identifying the molecular pathways of gene regulation by transcription factors and microRNAs in the immune system and in breast cancer
- Developing and using lentiviral technologies to over-express and knockdown target genes in primary human cells
- Developing cell-based therapies from cord blood stem cells

Myeloma Research Laboratory

Research Leader:
Associate Professor Andrew Zannettino

Multiple myeloma (MM) is an incurable haematological cancer of the antibody-producing plasma cell (PC). The frequency of this disease is estimated to be five to six new cases per 100,000 persons per year. MM is unique amongs haematological malignancies in its capacity to cause massive destruction of the skeleton. The focal osteolytic lesions result in a range of debilitating clinical symptoms including bone pain, pathological fractures, spinal cord compression, hypercalcemia and renal failure. The Myeloma Research group's efforts centre on identifying the molecular and cellular mechanisms responsible for myeloma disease progression.

Research Priorities:

- Determining the role played by hypoxia in MM disease progression
- Identifying novel bone marrow microenvironmental factors that may contribute to MM disease progression
- Identifying novel agents to inhibit osteoclast-mediated bone loss and/or stimulate osteoblast-mediated bone formation
- Identifying novel signalling pathways with roles in mesenchymal stem cell differentiation which may be manipulated to increase bone formation in MM patients
- Examining the skeletal and metabolic effects of tyrosine kinase inhibitor (TKI) compounds
- Developing aptamers (nucleic acid-based antibody-like molecules) directed against candidate molecules with roles in MM disease progression

Periodontal Repair

Research Leader: Professor Mark Bartold

To date, repair of damaged periodontal tissues relies on implantation of structural substitutes with little or no reparative potential. More recently, tissue-engineering, based on an understanding of the cell and molecular biology of the periodontium, has emerged as an interesting alternative to existing therapies for periodontal regeneration.

The Periodontal Repair group has established the presence of mesenchymal stem-like cells (PDLSC) in both human and ovine periodontal tissues capable of sustained renewal and tissue regeneration. The group now hypothesises that PDLSC can be used for cellular-based therapies to treat damaged periodontal tissues.

Research Priorities:

- Mesenchymal stem cells from the periodontal tissues for periodontal regeneration
- Production, characterisation and utilisation of iPS cells
- The utilisation of stem cell technologies to improve clinical periodontal regenerative techniques

Reproductive Biotechnology Group

Research Leader:
Associate Professor Mark Nottle

The Reproductive Biotechnology group has an international reputation in the general areas of reproductive biology and the development of associated technologies for biomedical and agricultural applications. In collaboration with a number of university, institute and hospital research groups in Australia as well as overseas, current research is focused on developing organ, tissue and cell replacement therapies. This work is funded by various agencies including the Juvenile Diabetes Research Foundation, the National Health and Medical Research Council and industry.

In 2009 the group presented its findings regarding the development of a new method for the isolation of mammalian embryonic stem cells including its use in isolating embryonic stem cells from the pig.

Research Priorities:

- Isolation and characterisation of various stem cell types from the pig. These will be used for a range biomedical and agricultural applications, as well as a model for human stem cell research.

Stroke Research

Research Leader:
Associate Professor Simon Koblar

The human brain is claimed to be the most complex 1.5 kg of matter in the known universe. There has been an incredible increase in understanding of the brain over the past 20 years, from imaging, physiological, cellular and molecular/genetic perspectives. The major challenge and goal of the Stroke Research group is to take this knowledge and exploit it to prevent and treat stroke better.

Stroke is by far the most common neurological disease, afflicting 60,000 Australians per annum. It is the second leading cause of death. A significant number of people are left with neurological disability and it remains the leading cause of adult disability in Australia.

In 2009 the group found that transplanted adult stem cells derived from human teeth resulted in a significant improvement in function following a stroke in rodents. The group injected these adult human stem cells into the rat brain 24 hours following a stroke, which caused a significant improvement in limb function four weeks following stroke as compared to animals with no stem cell treatment.

Research Priorities:

- Stem cell therapy in stroke
- Transcriptional regulation of stroke
- Stem cells and nanotechnology – investigating a 'neurochip'
- Models of care
- Neuro-imaging of the stroke brain

Transplantation Research

Research Leader: Dr Toby Coates

Research in the dendritic cell laboratory is focused on the induction of immunological tolerance for the treatment of organ transplant rejection. Haematopoietic stem cells are a significant and important source of pre-cursor cells for the generation of dendritic cells.

The major focus of the Transplantation Research group has been the development of novel pre-clinical transplantation models in which we can test tolerogenic therapies.

The future direction for research in the dendritic cell laboratory includes the application of this technology for pancreatic islet transplantation as well as other solid organ transplants.

CASE STUDY

EXPLORING NOVEL SOLUTIONS FOR TREATING DIABETES

Type 1 diabetes mellitus (also known as juvenile onset diabetes or insulin dependent diabetes) is a major health problem worldwide.

This disease damages tissues and organs, leading to a number of debilitating and potentially life-threatening complications, including premature heart disease, kidney failure (nephropathy), blindness (retinopathy) and poor circulation leading to strokes, gangrene and sometimes limb amputation. Diabetes mellitus is now the major cause of end stage renal failure in the world. Currently type 1 diabetes is treated by use of insulin injection, but this treatment is not a cure and requires lifelong therapy. Recently, new developments involving Dr Toby Coates and his research team have made transplantation of the insulin producing pancreatic islet cells a viable treatment option.

Treatment of Type 1 Diabetes with Islet Transplantation

Pancreatic islets make up only one to two per cent of the pancreas and are scattered throughout this organ. It is estimated there are approximately 1 million islets in a pancreas. In type 1 diabetes, the body‘s immune system mistakenly attacks and destroys the beta cells, and the body can no longer produce insulin. Recently, transplantation of islets that have been extracted from the pancreas has become possible. Put simply, the islets are removed from the donor pancreas via a complex laboratory procedure and subsequently transplanted into the recipient by injecting them into the liver via the portal vein.

Islet transplantation is just emerging from being experimental to becoming state of the art. It offers a number of advantages over whole organ (pancreas) transplantation in that no major surgery is required, and thus there is less risk to the patient and a much shorter recovery time. Patients typically leave the hospital in just a few days. In addition, the process can be repeated if necessary.

The goal of islet transplantation is to give back to type 1 diabetics the ability to produce insulin that is needed to regulate blood glucose levels by transplanting islets that actually produce insulin. Islet separation technologies allow these cells to be collected from a deceased donor‘s pancreas and transplanted into a recipient with diabetes at minimal risk to the patient, so he or she can produce sufficient insulin once again. With functioning islets, the release of insulin is continuous throughout the day in amounts that meet the body‘s requirements under the influence of glucose intake, as occurs in normal healthy individuals.

Returning blood glucose levels to normal will assist in preventing any further damage to a patient‘s cardiovascular, nerve or ophthalmic systems. There is also a possibility that any damage already present may improve over several years. In addition the non-diabetic state of the patients will stop any further damage to their kidneys that occurred while in their diabetic state.

Treatment of Brain Diseases Associated with Lysosomal Storage Disorders

Research Leaders:
Professor John Hopwood and Dr Kim Hemsley

More than 40 diseases are classified as lysosomal storage disorders (LSDs). Each results from an inherited genetic defect that causes an enzymatic deficiency or malfunction in the cell's lysosomes. The lysosome is involved in the breakdown and removal of waste from the cell. When loss of activity of an enzyme of the lysosome occurs, it impairs waste trafficking, causing cellular dysfunction.

Patients suffering from lysosomal storage disorders suffer from heart problems, breathing difficulties, stiff joints, skeletal deformities, enlarged heads and a characteristic facial appearance. Further, in some patients, this leads to the development of brain disease, causing mental impairment (leading to hyperactivity, aggressiveness and loss of learned skills such as walking and talking).

While individually most of these diseases are rare, as a group their incidence is about one in 7,700 live births.

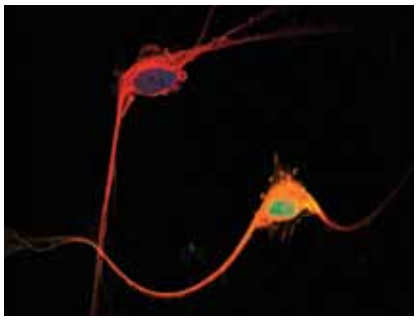
Research into lysosomal storage disorders that affect the CNS has also proposed the use of stem cells to treat these diseases.

The wider objective of this group is early diagnosis and effective therapy for all lysosomal storage disorder (LSD) patients. To this end, a number of genes have been systematically isolated that are involved in LSDs and characterised mutations that effect their efficient expression. This has lead to a number of studies to investigate the pathophysiology of these storage disorders, evaluation of a number of potential therapies and the development of technology to enable newborn screening for these conditions.

Understanding Neural Development in Mice and Man using Stem Cells

Research Leader:
Associate Professor Paul Thomas

The main focuses of the group are on the genetic causes of mental retardation in children and, in particular, on the role of X chromosome genes in brain function. The group has established mouse models for the mental retardation syndrome X-linked Hypopituitarism which are providing unique insights into the genetic control of brain development and the biological basis of mental retardation. These models are also powerful tools for identifying novel genetic regulators of brain development, through comparison of gene and protein expression in genetically modified and control animals.



The group also recently established a unique mouse model of sex reversal in which chromosomally female mice develop as males. These mice are providing exciting new insights into the evolution and molecular mechanism of sex determination in mammals.

Research Priorities:

- Using stem cells to identify the role of the SOX3 gene in brain development
- Using mouse models to identify and characterise new genes that cause intellectual disability and epilepsy
- Understand the role of SOX3 in sex determination in mice and man

AWARD & FELLOWSHIP HIGHLIGHTS

Professor John Hopwood
CSL Florey Medal

Danijela Menicanin
Best Research Poster "Comparative Genetic Profiling of Human Mesenchymal Stem Cell Derived from Bone and Dental Tissue". Presented at Faculty of Health Sciences Postgraduate Research Expo

Deborah Harland
Hanson Institute Clinical Researcher of the Year Award for 2009

Dr Sally Martin
HSANZ Albert Baikie Memorial Medal
University Medal

Dr Peter Psaltis
Hugh Gilmore Prize
Nimmo Prize
Ross Wishart Memorial Award

Dr Michelle Perugini
Shahin Early Career Research Fellowship

THE FUTURE

The Centre for Stem Cell Research will continue to contribute significantly to the wealth of scientific knowledge in stem cell research. The Centre will work towards increasing competitive grant funding to further build the capacity of our research and build on strategies to further promote a cross-disciplinary approach to research and maximise internal collaborative opportunities.

The Centre is looking to attract a leading scientist in the area of induced pluripotent stem cells in 2010-2011. As well as developing their own research programs in this area, this researcher will collaborate with several of the Centre's existing groups to develop this technology to deliver novel solutions for a number of currently incurable diseases.

The Centre for Stem Cell Research, together with the Robinson Institute, is looking to attract funding for various research initiatives through the recently formed Robinson Foundation and also the recently announced formation of the Peter Couche Foundation, which is focused on supporting leading research into the use of stem cells to repair stoke damaged brains.

Associate Professor Mark Nottle and Associate Professor Stan Gronthos

CASE STUDY

NEW HOPE FOR STROKE REPAIR

Exciting advancements at the Centre for Stem Cell Research are providing hope for thousands of Australians who suffer brain damage as a result of stroke.

The importance of this research is significant, with stroke being the leading cause of disability in Australia. More than 250,000 people are estimated to be living with the aftermath of strokes.

Associate Professor Simon Koblar, Director of the Stroke Research Program, says, "A major challenge before neuroscience is how to repair the brain following a stroke." The research is showing promising results regarding the use of adult stem cells from teeth to improve the brain functionality of victims of stroke.

Associate Professor Stan Gronthos, Co-Director of the Centre for Stem Cell Research, was one of the first to isolate stem cells from the adult human tooth. This discovery laid the foundation in Adelaide to use dental pulp stem cells for brain repair.

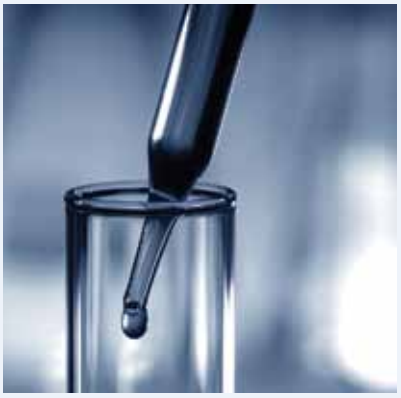
Various organs of the body, such as bone marrow, skin or teeth, have small numbers of adult stem cells that are able to regenerate specific organs' tissues.

The research has discovered that adult dental pulp stem cells have an intrinsic ability to produce brain cells and make a range of growth factors likely to help repair the brain.

The Catholic Archdiocese of Sydney awarded the group $100,000 through a competitive grant to progress the research using adult stem cells.

The Robinson Institute is working with University of Adelaide graduate and stroke victim, Mr Peter Couche, to raise awareness of and funding to continue this important research through the establishment of the Peter Couche Foundation.

Peter, a highly successful stockbroker, at 41 suffered an irreversible brain-stem stroke that left him paralysed but with an active and alert brain. His book, *Lifelines*, documents his life and the importance of discoveries such as stem cells to improve the lives of people affected by stroke.



"The best cell-therapy is one which is initially from the patient so no treatment is required to reduce the immune system and stop rejection."

Associate Professor Simon Koblar, above with Mr Peter Couche

250,000

Number of Australians estimated to be living with the aftermath of strokes.

Associate Professor Simon Koblar

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2009 PUBLICATIONS

Al-Mawali A, Gillis D, Lewis I. 2009, The role of multiparameter flow cytometry for detection of minimal residual disease in acute myeloid leukemia. *American Journal of Clinical Pathology* 131 : 16-26

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