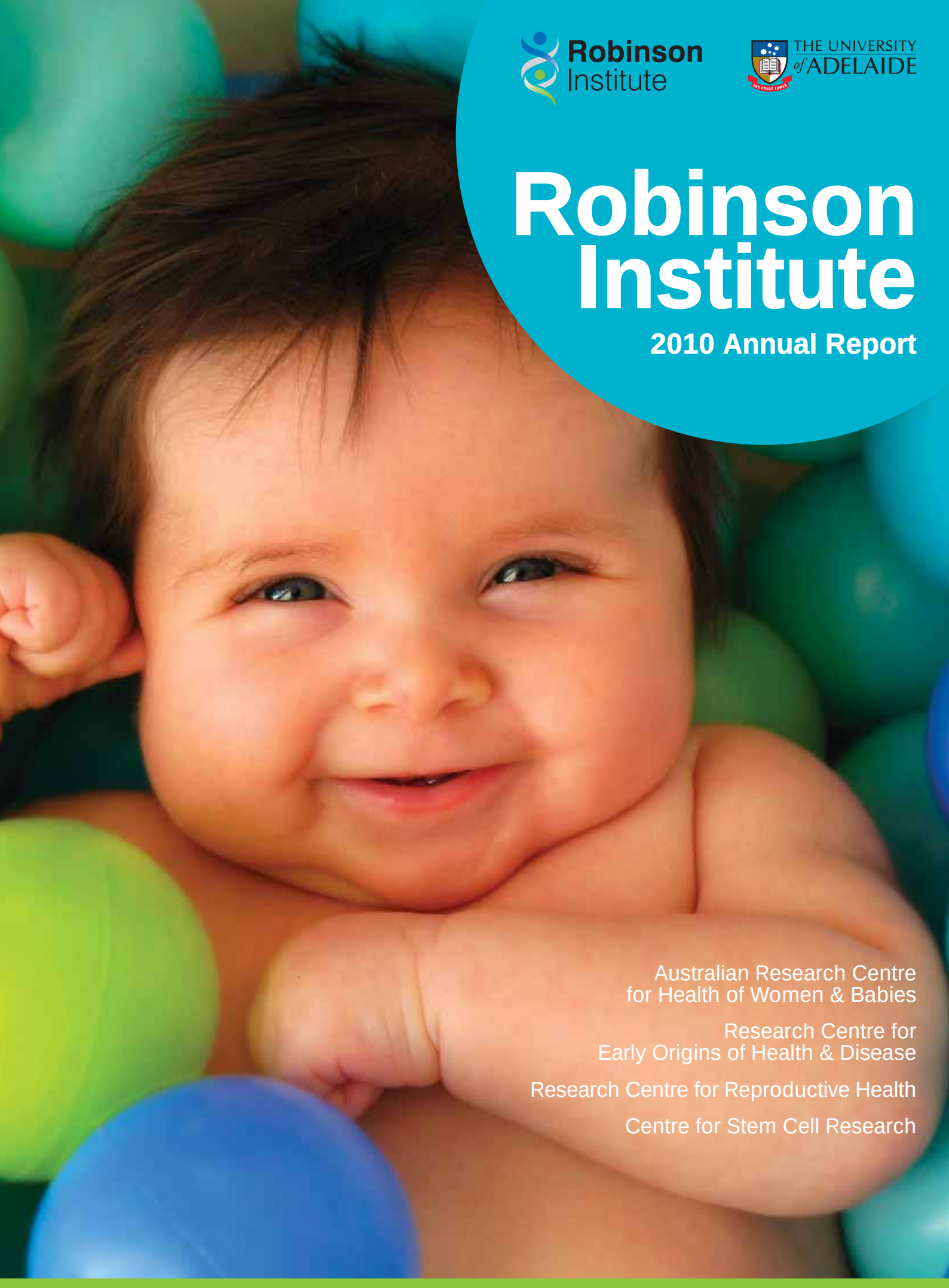

Robinson Institute

THE UNIVERSITY of ADELAIDE

Robinson Institute

2010 Annual Report

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

Sheree Lyon and her 6 month old son Samuel (courtesy The Advertiser)

WHO WE ARE

The Robinson Institute's driving focus is giving and sustaining life for existing and future generations – that is, creating life and making sure it's as healthy as possible throughout by finding cures and treatments for a range of health issues and illnesses.

The Institute was officially launched in 2009 to bring together four of the University of Adelaide's leading health research centres.

Our research covers the whole life spectrum:

- Conception and fertility, with a focus on helping people realise their hopes of starting a family
- Healthy start to life, where the focus is on healthy pregnancies and infants' early years
- Regenerative medicine, where we're looking at the use of stem cells to cure a number of illnesses and disabilities, including stroke and cystic fibrosis.

Our unique blend of more than 350 dedicated, world-class researchers have wide-ranging expertise and work tirelessly on a variety of relevant and groundbreaking programs. Some have been named among the nation's best and their international research breakthroughs have covered everything from IVF and fertility, to national guidelines for pregnancy health, and we are now also a step closer to preventing cerebral palsy.

One of our greatest strengths is the way we link clinicians and our researchers – which means improved sharing of ideas and outcomes, meaning faster and better results for the community and for future generations.

The Robinson Institute is driven by the belief that our work has major life impacts, with medical research holding the key to improving the health of future generations.

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HIGHLIGHTS 2010

Australia Day honour for Professor Alastair MacLennan

Professor Alastair MacLennan was appointed an Officer of the Order of Australia for his 40 years' work in women's and children's health, in particular unravelling the causes of cerebral palsy.

Expanding research facilities at the Lyell McEwin Hospital

The Institute opened the doors to new facilities at the Lyell McEwin Hospital, in the northern suburbs of Adelaide. The site houses a number of our researchers, in particular our Pregnancy and Development Group, and provides outreach to socially disadvantaged and Indigenous communities, where we feel our research into early life can have an enormous impact.

IVF breakthrough

Professor Sarah Robertson partnered with the Danish company Origio to develop a product which improves IVF embryo implantation rates for some women by up to 40%. The resulting product, EmbryoGen, to be released in 2011, contains a signalling molecule called GM-CSF found naturally in the mother's tissues which protects the embryo from stress, making it stronger and more robust in the early implantation period.

Growth in funding and publications

Robinson Institute members received over $16.3 million in income during 2010, primarily from Commonwealth funding schemes.

Over 300 papers were published, most in high impact factor journals including a paper published in the high profile journal Nature.

Robinson Foundation and Peter Couche Foundation

The Institute's two philanthropic streams, the Robinson Foundation and the Peter Couche Foundation, raised over $200,000 to further support our research activities.

During 2010, Peter Couche, founder of the Peter Couche Foundation, was awarded the Pride of Australia Medal for Courage for his determination and strength of character to overcome personal adversity. The Peter Couche Foundation raises funds for the Stem Cell for Stroke Research Program of the Institute.

Our researchers recognised

Our researchers were recognised for their important contribution to society through numerous public awards in 2010, including Officer of the Order of Australia, Ross Wishart Memorial Award, South Australian Young Investigator Award, Future Justice Prize, and SA Young Tall Poppy of Science.

Excellence in Research for Australia (ERA) results

Under the research area of paediatrics and reproductive medicine, the University of Adelaide was the only university in Australia to achieve a maximum score of 5, ranking it highest in the nation under the Federal Government's Excellence in Research for Australia initiative. The score ranks this research area well above world standard, confirming that the Robinson Institute and the School of Paediatrics and Reproductive Health has established a foundation for current and continuing world-class research.

(L) Associate Professor Simon Koblar

CHAIRMAN'S & DIRECTOR'S REPORT

The Robinson Institute works in one of the most important areas of medical research, namely the start of life, from conception and pregnancy through to early development and the origins of diseases. The incorporation of stem cell research allows us to look at the whole life spectrum and explore innovative technologies in regenerative medicine.

Our research has the potential to revolutionise both medical practice and personal care with the hope of finding preventions, treatments and cures for health conditions, from infertility and childhood diseases to cancer and stroke.

We have a large and ambitious research agenda and we are proud of the depth of talent in reproductive health and regenerative medicine found within the Institute. Through our research we are creating life, ensuring the best start for healthy living and saving lives.

Strategy and growth

Our strategic plan is built around four key objectives:

- Building an outstanding research profile
- Maintaining a strong funding base
- Attracting and retaining quality researchers
- Creating a dynamic working environment.

In the second year since the Institute's establishment, we have seen continued growth of our organisation and the development of a number of key initiatives that support our strategies.

Achievements

Individuals within the Institute had great success in 2010: Professor Alastair MacLennan was awarded an Order of Australia for his pioneering work in cerebral palsy and women's health; Dr Kylie Dunning won the prestigious Young Investigator Award; and other members of the Institute won numerous prizes and had high impact publications.

Our maximum score of 5 in the recent Excellence in Research for Australia (ERA) review by the Federal Government highlights the pre-eminence of paediatrics and reproductive health in Adelaide, which is built on quality staff and students and is producing high quality research outcomes.

Growing research and capacity

Robinson Institute member income increased to over $16.3 million, primarily through Commonwealth funding schemes. Our research output was also significant with over 300 papers published, most in high impact factor journals.

A core objective of 2010 was to increase research support services to build our capacity and ensure our personnel are productive and fulfilling their potential.

Retaining and recruiting outstanding staff and students and then supporting them by appropriate programs and administrative backup are essential for the success of any institute. Throughout the year we established professional development and mentoring programs for researchers; encouraged productivity through awards, prizes and collaborative programs; and worked with the School of Paediatrics and Reproductive Health at the University of Adelaide to ensure appropriate and efficient research support services.

Through our programs we have sought to encourage the individuality of our researchers while at the same time encouraging a collaborative approach.

Establishing new integrated facilities

In 2010 the Institute opened new facilities at the Lyell McEwin Hospital. This site accommodates a number of our researchers and provides an opportunity to engage members of the community in our clinical research programs.

We also have a number of projects in development to upgrade current laboratory facilities at the Medical School at the University of Adelaide and to establish new clinical teaching facilities on the Women's and Children's Hospital site.

Board of Governors

In 2010 the Board of Governors welcomed two new members: Mr Ian Nightingale and Professor Jonathan Morris. Mr Nightingale joined through his position as Chair of the Robinson Foundation. This provides a vital link between the two boards and highlights the importance of community support and engagement to the Institute. Professor Morris, the Head of Obstetrics and Gynaecology at the University of Sydney, brings a wealth of research and clinical practice expertise.

Mr Mark Coleman (L) & Professor Robert Norman

We would like to recognise the important contribution of the Board, their continued support and their invaluable guidance to our Director, senior management and wider Institute membership.

Future

In 2011 the Robinson Institute will undergo its first external review. This will be an important process, and will allow us to reflect on our achievements to date and then help us to implement a robust and innovative strategy to build this great organisation.

The ongoing challenge for the leadership of the Institute is to ensure that our structures and programs continue to support both individuals and those collaborative enterprises that are so essential for success in modern medical research.

The Institute is continually exploring various avenues to improve capacity and infrastructure, as well as to diversify our funding opportunities.

At the Robinson Institute, we not only measure our success on the growth in funding and research publications, but on how our research is having real-life impact in the community through ensuring that the discoveries of the Institute are translated into health practices that benefit the wider community and the health of future generations.

Mr Mark Coleman, Chairman
Professor Robert Norman, Director

BOARD OF GOVERNORS

Mr Mark Coleman (Chairman) has been a practicing director for over 20 years, serving on over 20 Boards during that time, across private, public and not-for-profit sectors and across a wide range of industries, including chairing a number of these Boards and Board Committees. Mark undertakes governance reviews for a range of clients, is a long-standing national facilitator in the director-education programs of the Australian Institute of Company Directors, and continues to consult in the area of organisational strategy

Professor Justin Beilby is the Executive Dean of the Faculty of Health Sciences at the University of Adelaide and has been involved in research and evaluation with workforce planning, primary care financing, chronic illness and the Quality Use of Medicines for over twenty years, in both urban and rural settings. Prof Beilby is currently a member of the South Australian Health Performance Council and a Director on the South Australian Health and Medical Research Institute Board. He has been a member of the Medical Services Advisory Committee and the Strategic Research Initiatives Working Group of the National Health and Medical Research Council.

Professor Mike Brooks is the Deputy Vice-Chancellor and Vice-President (Research) at the University of Adelaide and is a leading international researcher in computer vision and image analysis. Prof Brooks' work has seen wide commercial use in the security and defence industries and has resulted in international awards. Prof Brooks is a Fellow of the Australian Computer Society and the Australian Academy of Technological Sciences and Engineering, Co-Investigator with the Australian Research Council Research Network for a Secure Australia, Associate Editor of the International Journal of Computer Vision, and serves on the Board of National Information and Communications Technology Australia and the National Computational Infrastructure Steering Committee.

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Dr Marie Dziadek is a biomedical research scientist and academic with expertise in developmental biology, mammalian embryology, cell and molecular biology and cancer biology. Dr Dziadek has extensive experience in research management and research review. She has participated on project grant and fellowship review panels, and has set up internal institutional grant review processes to provide mentorship in grant-writing. She is currently General Manager (Australia) for Academic Search International, an executive search firm specialising in recruitment of senior academics and leaders in the higher education sector.

Professor Jock Findlay is Head of the Female Reproductive Biology Group at Prince Henry's Institute in Melbourne as well as Director of Research at the Royal Women's Hospital in Melbourne. Prof Findlay was made a Member of the Order of Australia (AM) in 2001 and an Officer of the Order of Australia (AO) in 2007 by the Government of Australia, "for services to medical research, particularly reproductive biology, and as a medical administrator."

Professor Tanya Monro is an Australian Research Council Federation Fellow and Director of the Institute for Photonics & Advanced Sensing (IPAS) at the University of Adelaide. The vision of IPAS is to pursue a transdisciplinary research agenda, bringing together physics, chemistry and biology to create knowledge and disruptive new technologies, and solve problems for health, defence, the environment, food and wine. Prof Monro is also Director of the Centre of Expertise in Photonics (CoEP) within the School of Chemistry & Physics. Prof Monro is South Australia's 'Australian of the Year' for 2011 and in 2010 she was named South Australian Scientist of the Year.

Professor Jonathan Morris is Professor of Obstetrics and Gynaecology, Associate Dean and Head of the Medical School Northern at the University of Sydney. Prof Morris is also Head of Perinatal Research at the Kolling Institute, University of Sydney. The Perinatal Research Division was awarded a National Health and Medical Research Council Centre for Clinical Research Excellence in 2010 and spans basic science, clinical and population health research.

Mr Ian Nightingale joined the Board of Governors in 2010 through his role as Chair of the Robinson Foundation. Additional details can be found on pg 7.

Mr Phil Robinson is Executive Director Acute Services at the Children Youth and Women's Health Service (CYWHS) where he has responsibility for management of the acute service divisions within the Women's and Children's Hospital in Adelaide. Phil is a clinical psychologist by profession who has extensive management experience in both community and hospital settings. In 2004, Phil was awarded the Public Service Medal (PSM) in the Australia Day Honours List for his services to child and adolescent mental health.

Professor Paul Rolan is Professor of Clinical Pharmacology at the University of Adelaide. Prior to taking up this position in 2005, Prof Rolan had 18 years experience in the corporate sector in the United Kingdom, initially for a major pharmaceutical company and then as Medical Director of a University of Manchester 'spin-out' clinical research company. In Adelaide, Prof Rolan jointly established the Pain and Anaesthesia Research Clinic (PARC) within the Royal Adelaide Hospital which attracts international funding for commercial clinical trials supporting academic research.

Professor Bik To is the Clinical Director of Haematology at SA Pathology, which covers haematology services for all SA Pathology sites. Previously, Prof To was Head of Haematology for the Royal Adelaide Hospital/Institute of Medical and Veterinary Science campus. Prof To's group pioneered the mobilisation of autologous peripheral blood haemopoietic progenitors and over 15 years laid the scientific and clinical foundations for peripheral blood stem cell mobilisation and transplantation and was recognised by the inaugural SA Great Health Award in 1998. His Department has world leading research teams in leukaemia, mesenchymal stem cells and apoptosis.

ROBINSON FOUNDATION CHAIRMAN REPORT

In our inaugural year the Robinson Foundation made important steps to establish our structure and governance arrangements while also developing strategies to build a strong philanthropic and community engagement framework for the Robinson Institute.

The Foundation was officially launched in February 2010 at a memorable gala dinner in the grounds of Government House. This event introduced over 250 people to the inspiring research being carried out at the Institute and marked the first fundraising initiative of the Foundation. The involvement of our new Patrons, His Excellency Rear Admiral Kevin Scarce AC CSC RANR, Governor of South Australia, and Mrs Liz Scarce, was announced at our launch, and I would like to thank His Excellency and Mrs Scarce for their genuine interest and ongoing support for the activities of the Robinson Institute and the Robinson Foundation.

In October, His Excellency toured the Institute's research facilities at the University of Adelaide's Medical School. This tour highlighted the groundbreaking research being conducted and the incredible depth of talent we have here in South Australia.

During 2010, we focused our efforts on establishing the necessary structures and legal arrangements for the Foundation, and expanded our Board to bring together a range of skills and perspectives to the Foundation. Importantly, our Board members' linkages into the business community provide us with the opportunity to raise awareness and the profile of the Robinson Institute and Foundation.

Along with founding members of the Foundation, we welcomed four new members: Ruth Vagnarelli, Julie Mitchell, Neil Howells and Stephen Couche (through his position as Chair of the Peter Couche Foundation). I would like to recognise the significant contribution of all Board members – their enthusiasm, time and commitment given to supporting the research of the Institute should be truly commended.

We are committed to ensuring that the Foundation's fundraising activities are conducted with clear and transparent practices. We worked closely with the Legal & Risk and Development & Alumni departments of the University of Adelaide to finalise agreements on these practices and we would like to recognise their continued support of the Foundation.

A core focus for the Foundation is raising awareness of the Institute's research outcomes. The marketing plan prepared by our small but dedicated team sets out an ambitious program to reach the broader community and is already paying dividends with a number of high profile media opportunities showcasing the work of the Institute. Examples of other more targeted opportunities have included Professor Alastair MacLennan and Dr Kylie Dunning presenting to two enthusiastic Rotary groups about their research into cerebral palsy and fertility preservation in female cancer survivors, and our collaboration with the University's Development & Alumni department for a Friends and Benefactors research seminar.

The Foundation welcomed the invitation to become involved in the National Wine Centre's fortnightly themed "Uncorked" program, firstly with Tim Adams Wines in November, and then in the final event of the year where patrons celebrated Christmas with Bollinger. At both events, the Robinson Foundation received part of the proceeds of each glass and bottle of wine purchased.

By the end of 2010, the Robinson Foundation had accumulated $207,000 from fundraising activities. Of this, a significant component was directed towards the Peter Couche Foundation which successfully raised over $153,000. The Peter Couche Foundation sits within the Robinson Foundation and specifically supports the Robinson Institute's research into using adult stem cells for stroke treatment. The Peter Couche Foundation team is a driven and enthusiastic group and should be commended for their dedication to this worthwhile cause, as stroke could touch any of our families' lives without warning.

The year ahead ...

With many of the establishment activities now behind us, the Robinson Foundation Board and staff members can look forward to an exciting year where our efforts to date will begin to yield greater results. This really is a team effort, requiring both the energy and commitment of Board members and staff, and I would specifically like to acknowledge the tireless efforts of Jo Close and Alissa Nightingale in bringing together so many of the elements outlined above.

Just as we have been committed to getting our governance arrangements in place throughout 2010, I see 2011 as the year when we build on that solid work to put in place fundraising and partnering strategies to engage, inspire and empower the community to become involved in the Foundation and the Institute.

Importantly, the funds we raise through our Foundation go directly into our research programs and will deliver real and meaningful results. In 2011, the Foundation will make its first call for applications for funding from researchers of the Institute. We look forward to reporting back to our supporters on the outcomes of this investment in research.

In closing, I am proud to be involved in an organisation that believes in delivering a healthier future for our community. I am constantly moved by the stories that sit behind the research, and astounded by the quality of the research being undertaken in South Australia that will have national and international applications.

Mr Ian Nightingale, Chairman

ROBINSON FOUNDATION BOARD

Ian Nightingale is Chair of the Robinson Foundation Board as well as the first Chief Executive of the Department of Planning and Local Government. The department was established with a charter of achieving planning reform and economic development. Since Ian's appointment in November 2008 he has managed reform of the planning system through a range of urban development and planning initiatives, delivered a revised State Planning Strategy through the 30-year Plan for Greater Adelaide, fostered high-level planning coordination across State Government agencies and developed strong, collaborative partnerships with local government and industry.

Robyn Brown has been the Director, Development and Alumni at the University of Adelaide since August 2006. Robyn leads a committed team in the development and implementation of the University's Philanthropic and Alumni Engagement program. Robyn's fundraising, communications and marketing experience was gained from various roles over a 14 year period in both not-for-profit organisations and in the corporate sector.

Stephen Couche recently retired as Managing Director of Orlando Wines and as a Director of its parent company Premium Wine Brands. He remains on the management committee of Premium Wine Brands. Stephen joined Orlando Wines in 1974 and has overseen the international development of Jacob's Creek since its launch in 1976.

Sathish Dasan is a Partner of Norman Waterhouse lawyers and in charge of the firm's Employment and Local Government Governance and Regulatory Services Teams. For well over a decade, Sathish has been one of local government's pre-eminent employment law specialists. Over that time, he has expanded his area of interest and expertise to include all aspects of governance and probity concerning public institutions and its officers.

Neil Howells is Partner of Hudson Howells, a South Australian based strategic management consulting firm which was established in1993. Its major focus is providing special assistance to government and corporate clients in strategic planning and business planning; economic and industry development; market planning and market research; export market development and customer relationship management.

Tim Hughes is the Managing Director of Hughes Public Relations Communication Counsel. Tim has more than 25 years' experience in media and public relations and has operated one of Adelaide's leading consultancies for almost 20 years, in which time he has focused the consultancy on developing strong relationships with clients, ensuring activities are aligned with clients' business plans and positioning aspirations as a means of ensuring positive brand development. Some of the areas of Tim's expertise are brand development, media liaison, corporate positioning and community relations.

Colin Matthews is an Emeritus Professor at The University of Adelaide, having been Professor of Reproductive Medicine 1987-1999. Prof Matthews is a Founding Director of The Pipette Company Pty Ltd and Reproductive Health Science Pty Ltd and has been a Board Member of the Channel 7 Children's Research Foundation in South Australia since 2003. In addition, Prof Matthews is a Director of Flinders Reproductive Medicine Pty Ltd, a non-profit organisation providing reproductive services and supporting reproductive research at Flinders University.

Julie Mitchell has 20 years experience in the corporate sector, working in the areas of strategic communication; designing and delivering complex and large scale communication strategies and programs, and corporate social responsibility; developing strategy, designing and implementing programs, with an Australian and Asia Pacific focus. Recently, Julie developed and implemented Santos' enhanced community investment program in South Australia including their first involvement as principal sponsor of the Tour Down Under.

Mary Patetsos is Chair of the South Australian Local Government Grants Commission as well as a member of the of South Australia's Social Inclusion Board and the Board of the South Australian Housing Trust and South Australian Affordable Housing Board. Mary also acts as Chair of the external Audit Committee of the South Australian Department of Families and Communities and is a Director on a number of not-for-profit boards in South Australia. Mary's current positions enable her to have extensive knowledge of the economic, infrastructure and social needs of South Australia.

Ruth Vagnarelli is Design Director for the Hickinbotham Group and works closely with architects to develop new housing ranges including sustainable and energy efficient designs and affordable housing. An Arts graduate from the University of Adelaide, Ruth is a journalist, an experienced marketer and has also studied interior design. Ruth is actively involved in the residential housing industry and is a member of the Housing Industry Association's South Australian Regional Executive Committee.

Dr Julia Pitcher, Ryan Higgins, Luke Schneider and John Drysdale

The Robinson Institute brings together a unique blend of more than 350 researchers and clinicians

MANAGEMENT COMMITTEE

Professor Robert Norman is Director of the Robinson Institute and holds a personal chair as Professor for Reproductive and Periconceptual Medicine at the University of Adelaide and is a subspecialist in reproductive medicine (CREI) and in endocrine biochemistry (FRCPA). He is leader of the NHMRC Program Grant on 'Periconceptual origins of health and disease' and has published over 330 peer-reviewed publications and one book.He serves on the editorial board of major journals as well as National Health and Medical Research Council's research and embryo licensing committees.

Prof Norman's major research contributions have been in IVF and reproductive endocrinology, particularly in PCOS, the effect of lifestyle on reproductive outcomes and periconception medicine. He is an active reproductive medicine specialist.

Joanna Close commenced with the Robinson in early 2009. Her experience in the bioscience sector has been diverse and includes: initiating a $3.3 million collaborative program to facilitate medical device product development in South Australia; designing methods and analysing results for South Australia's first bioscience research and industry survey; and providing support to South Australia's first bioscience angel investment group.

Jo's formal qualifications are in Biotechnology for which she was awarded first-class Honours. In 2010 she graduated from the Governor's Leadership Foundation Program.

Professor Julie Owens is Head of the School of Paediatrics and Reproductive Health at the University of Adelaide and Co-Director of the Research Centre for Early Origins of Health and Disease.

Prof Owens' research seeks to increase fundamental knowledge about early growth and development and how it is altered in major pregnancy complications, especially growth restriction and its impact on health and risk of disease long term.

Associate Professor Michael Ridding is Co-Director of the Research Centre for Early Origins of Health and Disease and in 2008 was awarded a National Health and Medical Research Council Senior Research Fellowship. A/Prof Ridding jointly heads the Neuromotor Plasticity and Development (NeuroPAD) research group and is internationally-renowned for his pioneering work in human brain plasticity induction.

Associate Professor Michael Davies is Co-Director of the Research Centre for Early Origins of Health and Disease as well as an Australian Research Council Future Fellow. A/Prof Davies co-directs the Life course and Intergenerational Health Research Group which is a multi-disciplinary group which works primarily within research domains that are having increasing impact on concepts of health and disease aetiology, treatment and prevention.

Associate Professor Jeremy Thompson is Co-Director of the Research Centre for Reproductive Health as well as a National Health and Medical Research Council Senior Research Fellow. A/Prof Thompson is the Research Program Leader of the Early Development Group and his research interest lies in the impact of the micro-environment, especially nutritional factors, surrounding the cumulus-oocyte complex and early embryo in establishing oocyte competence and embryo develop-ment potential, in both the in vivo (follicular/oviduct/uterine) or in vitro environment.

Professor Sarah Robertson is Co-Director of the Research Centre for Reproductive Health as well as a National Health and Medical Research Council Principal Research Fellow. Prof Robertson is the Research Program Leader of the Reproductive Immunology Research Group and her research interest is early pregnancy, and the significance of immune events occurring in early pregnancy on fetal development and health after birth.

Professor Caroline Crowther is Director of the Australian Research Centre for Health of Women and Babies as well as a Maternal Fetal Medicine Sub-specialist. Prof Crowther leads many large multicentred randomised clinical trials and research synthesis and translational and implementation projects that focus on the evaluation of new perinatal therapies or care practices, in collaboration with researchers in key institutions in Australia, New Zealand and overseas.

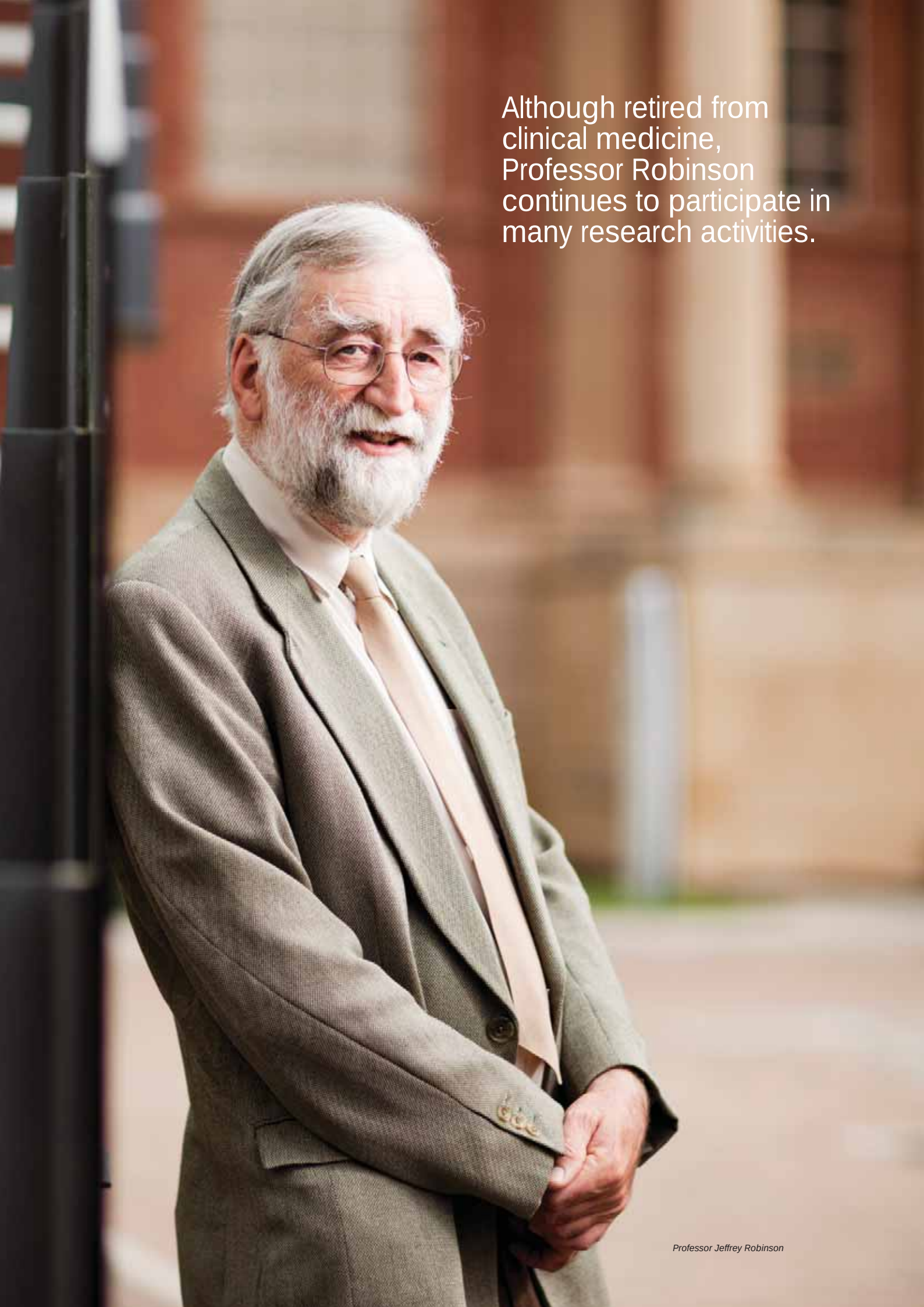
Professor Jodie Dodd is Co-Director of the Australian Research Centre for Health of Women and Babies and leads a multidisciplinary research group undertaking a large randomised trial evaluating the effect of a dietary and lifestyle intervention for pregnant women who are overweight or obese.

Prof Dodd is also a Fellow of the Royal Australian and New Zealand College of Obstetrics and Gynaecology as well as a Maternal Fetal Medicine Sub-specialist at the Women's and Children's Hospital in Adelaide.

Ms Philippa Middleton is Co-Director of the Australian Research Centre for Health of Women and Babies and a perinatal epidemiologist specialising in evidence-based and translational health methods, including development and implementation of clinical practice guidelines. Philippa heads the Centre's National Health and Medical Research Council (NHMRC) Evidence Panel and is a Chief Investigator of four NHMRC project grants.

Associate Professor Mark Nottle is the Co-Director of the Centre for Stem Cell Research as well as the Research Program Leader of the Reproductive Biotechnology Group which has an international reputation in developing reproductive biotechnologies for agricultural and biomedical applications. Current research is focused on isolating embryonic stem cells in the pig for various applications including the development of a much needed large animal model for bridging the gap between mouse studies and human clinical trials.

Professor Stan Gronthos is the Co-Director of the Centre for Stem Cell Research as well as a National Health & Medical Research Council Senior Research Fellow. Prof Gronthos' research activities have resulted in several highly cited seminal publications describing the identification, purification and characterisation of different mesenchymal stem cell populations from bone marrow, adipose and dental tissues. These cells are currently being used in different orthopaedic and cardiovascular pre-clinical and clinical studies.



Although retired from clinical medicine, Professor Robinson continues to participate in many research activities.

Professor Jeffrey Robinson

ORIGINS OF THE ROBINSON INSTITUTE

The basis for the Robinson Institute was laid in 1960 when Professor Lloyd Cox became the first Professor of Obstetrics and Gynaecology at the University of Adelaide, based at The Queen Elizabeth Hospital in Adelaide. Over the next two decades Professor Cox built an inspiring department that specialised in reproductive medicine and infertility.

A second University presence was established at the Queen Victoria Hospital in Dulwich, Adelaide, where most of the obstetrics was practised under the diligent care of outstanding staff specialists and academic obstetricians. Professor Cox, followed by Professors Matthews and Kerin, established a world-renowned infertility service and research enterprise, which included outstanding scientists such as Bob Seamark, Lou Warnes and many excellent embryologists.

In the early days, much of the emphasis was on steroid analysis and assays, with the need for good measurement for ovulation induction and donor insemination. Professor Matthews established one of the first donor sperm banks in the world, at The Queen Elizabeth Hospital, and subsequently became the first Professor of Reproductive Medicine at the University of Adelaide.

The Queen Elizabeth Hospital department was one of the first in the world to establish IVF pregnancies in the early 1980s. It went on to become the third in the world to have intracytoplasmic sperm injection (ICSI) pregnancies and the first in Australia to have pre-implantation diagnosis pregnancies. Under the care of Professor Matthews, the department grew its IVF and infertility profile and brought in outstanding clinicians and scientists to boost its research ability. Within a few years of the first Professor of Reproductive Medicine, the department had several project grants and soon had a program grant from the National Health and Medical Research Council (NHMRC).

Meanwhile, at the Queen Victoria Hospital, plans were being made to move to the more central Women's and Children's Hospital site. During this time Professor Jeffrey Robinson became Head of the Department of Obstetrics and Gynaecology.

A major presence was also established at the University of Adelaide Medical School, where a whole floor was devoted to laboratory-based research. For nearly 20 years the department ran a reproductive medicine program under the name of Repromed Pty Ltd, whereby all the profits from an outstanding clinical program where returned to research and development in reproductive medicine and obstetrics and gynaecology. Today some of our researchers continue to remain part of Repromed, which is a privately owned organisation.

It was on the basis of these outstanding personalities, a good funding model and excellent vision that one of the best departments of obstetrics and gynaecology in the world was built.

In 2006, the department left The Queen Elizabeth Hospital and moved to the Medical School and to the Women's and Children's Hospital. In the meantime, a major node had been established at the Lyell McEwin Hospital and a presence had always been held at the Royal Adelaide Hospital.

In 2007, Professor Robert Norman and Professor Julie Owens started to discuss the concept of an institute to encompass more than just obstetrics and gynaecology. Over the next two years they were able to encourage researchers in the areas of reproductive health, developmental origins of health and disease, stem cell technology and perinatal research to combine to form the Robinson Institute. On 1 October 2008 the Robinson Institute was born, under the leadership of Professor Norman and the management guidance of Directors of the four major centres: the Research Centre for Reproductive Health, the Australian Research Centre for Health of Women and Babies, the Research Centre for Early Origins of Health and Disease, and the Centre for Stem Cell Research. The Institute has brought together people from very diverse disciplines, ranging from basic cellular molecular biology through to public health, epidemiology and translational medicine.

Emeritus Professor Jeffrey Robinson

The Robinson Institute is named after Emeritus Professor Jeffrey Robinson. Professor Robinson was born in Northern Ireland, graduated from Queen's University Belfast in 1967 and, after establishing a research career at the University of Oxford, was appointed Professor of Reproductive Medicine at the University of Newcastle in 1980.

He was then appointed Professor of Obstetrics and Gynaecology at the University of Adelaide in 1996 following the retirement of Professor Lloyd Cox and served as Head of Department of Obstetrics and Gynaecology until 2006. During this time Professor Robinson was integral in developing and promoting the University of Adelaide's outstanding reputation for excellence in research in obstetrics, gynaecology, and reproductive medicine and biology.

Professor Robinson's research examines the control of fetal and placental growth and development, with his focus on the effects of placental restriction, insulin-like growth factors and nutrition on fetal growth. He is also interested in how events before birth may predispose the individual to common adult diseases such as high blood pressure.

In addition, he has conducted clinical studies including trials relating to mild gestational diabetes, induction of labour, and repeat dose corticosteroids before anticipated preterm. The outcomes of some of these studies have already been incorporated into national and international clinical guidelines, and have improved clinical practice and consequently health outcomes.

Although retired from clinical medicine, Professor Robinson continues to participate in many research activities.

Professor Robinson is internationally renowned and has published extensively in the area of fetal–maternal physiology. He has also enjoyed a distinguished career, receiving numerous awards including a Commander of the British Empire (CBE) in 2006 and the Women's Hospitals Association Medal of Distinction. An Honorary Life Member of the British Association of Perinatal Medicine, Professor Robinson has also served as the president of the Federation of Australian, Asian and Oceania Perinatal Societies.

RESEARCH THEMES

Securing and protecting fertility

Reproductive health and fertility researchers at the Institute are giving new hope to the one in four couples who have trouble conceiving.

Most couples take for granted that they will face no barriers to conceiving, they will enjoy a positive pregnancy and they will give birth to healthy children. But for those unable to achieve this dream, the difficulties can lead to frustration and heartbreak.

Our research covers the whole life spectrum starting with conception. Our experts believe that every family should have the best chance to conceive a child and they are working to gain better understanding of the conception process, both natural and assisted.

Other targeted research areas include:

- New IVF technologies (including the establishment of fertility clinics in South Australia)
- Reducing the risk of miscarriage
- Fertility diseases including endometriosis and polycystic ovary syndrome
- Fertility preservation for female cancer survivors
- Health of mother and father before conception
- Breast and ovarian cancer research.

In a recent breakthrough, the Institute's Professor Sarah Robertson and her team have developed a new product that will help millions of women around the world who suffer miscarriage after IVF treatment. The product, the result of 20 years' work and the world's largest clinical trial on IVF media, improves IVF embryo implantation rates by up to 40% for some women.

Our researcher Dr Kylie Dunning received the 2010 Young Investigator Award for her work to help preserve the fertility of female cancer survivors. Other researchers are promoting how lifestyle factors, such as obesity, smoking, drugs and stress, contribute significantly to infertility.

Impact of healthy pregnancies and the early years on future health and wellbeing

Researchers at the Institute believe that each baby born has the right to the very best start in life. Our researchers know that events around the time of conception, pregnancy and early childhood determine an individual's health and disease in later life. Research is also showing that factors during a mother's pregnancy can influence her daughter's reproductive and general health 30 years later, and researchers are investigating potential ongoing effects on the following generation.

To address these questions, one of our core program areas focuses on the health of women and babies and the early origins of health and disease. What we are learning and implementing is making meaningful differences for women and babies, and their families.

In an important breakthrough, the Institute's Professor Claire Roberts has been working with pregnant women to understand why some pregnancies end in complications that have major impacts for mothers and babies. Professor Roberts and her team are developing a world-first genetic test to predict which pregnancies are at risk of complications, long before symptoms arise. They have identified subtle variations in specific genes within the mother, father or baby that indicate the mother is more likely to suffer pregnancy complications. This research will lead to tailored and potentially lifesaving antenatal care.

In another important project, our researchers are carrying out a number of groundbreaking studies into prevention of cerebral palsy, a disease affecting one in 500 Australian children. They are trying to better understand the genes that are responsible and the other environmental factors that trigger this disease.

Other targeted research areas include:

- Maternal care before, during and after pregnancy and childbirth
- Early origins of health and disease (including diabetes, cerebral palsy, obesity and cancer risk)
- Minimising the impact of preterm birth
- Indigenous health
- Intergenerational health
- Maternal stress and sex differences in perinatal growth and survival
- Impact of nutrition and the environment on health outcomes.

Regenerative medicine – finding cures through stem cell research

New treatments and cures for many of the world's common diseases and disabilities, including stroke, leukaemia and cystic fibrosis, are a step closer to reality. These and other potentially life-saving and life-changing studies are being undertaken by our Centre for Stem Cell Research teams.

Our dedicated teams undertake internationally recognised and awarded research in bone marrow, neural, periodontal, ovarian and cord blood stem cells. They are working on how these cells can be used in a range of areas including repair of the body after stroke, and regeneration of tissues and organs affected by a host of inherited and immune diseases and disabilities.

In an important breakthrough, the Institute's Associate Professor Simon Koblar is carrying out research with potential impacts for the 60,000 Australians who experience strokes each year. His team's research is showing promising results in the use of adult stems cells from teeth to improve brain function after stroke.

In another world-leading project, researchers are investigating a groundbreaking treatment for the genetic disease cystic fibrosis, which affects about 3000 Australian children and young adults by attacking the body's organs, particularly the lungs. The outcome has the potential to improve lung function and provide a better quality of life for these patients.

Other targeted research areas include:

- Diabetes
- Leukaemia and other cancers
- Blood disorders
- Organ transplants
- Cardiac and bone repair.

Alison Care

Our research covers the whole life spectrum starting with conception.

CORPORATE REPORT

Research facilities and infrastructure

Ensuring quality facilities and infrastructure are available to researchers of the Robinson Institute is always high on our agenda. The best research is conducted using state-of-the-art equipment in purpose-built laboratories. The use of new technologies and processes can transform our research endeavours – making our research processes more efficient, more accurate and more detailed. This means we can get more meaningful results and get them faster. It also opens doors to new avenues of research – new ways of looking at problems, new ways of bringing together information and, ultimately, new solutions.

In 2010, the Robinson Institute opened the doors to new facilities at the Lyell McEwin Hospital in the northern suburbs of Adelaide. The Lyell McEwin is a significant site for a number of our researchers and provides a fantastic opportunity to engage members of the community in our clinical research programs. It provides outreach to socially disadvantaged and Indigenous communities, where we feel our research into early life can have an enormous impact.

Our interaction with clinicians within hospitals has always been an important focus for the Institute. Clinicians and clinical academics bring relevance to our research programs – they ensure that the research we do has the benefits expected by patients and members of the community. They understand the real problems, and help us apply science to create solutions.

The Lyell McEwin is another great example of our integration with the clinical community. By establishing research facilities on the site, we are not only providing laboratories for our researchers to work with samples collected from within the hospital, but we are also opening doors for clinicians within the hospital to engage in research activities. Associate Professor Vicki Clifton, Head of our Pregnancy and Development Group, manages our facilities on the site and is building relationships with clinicians that will no doubt drive new and exciting research programs.

It is just as important that we continue to improve our current facilities. There are other projects already underway: upgrading of our laboratories on the Medical School site at the main campus of the University of Adelaide, and the establishment of new clinical teaching facilities on the Women's and Children's Hospital site.

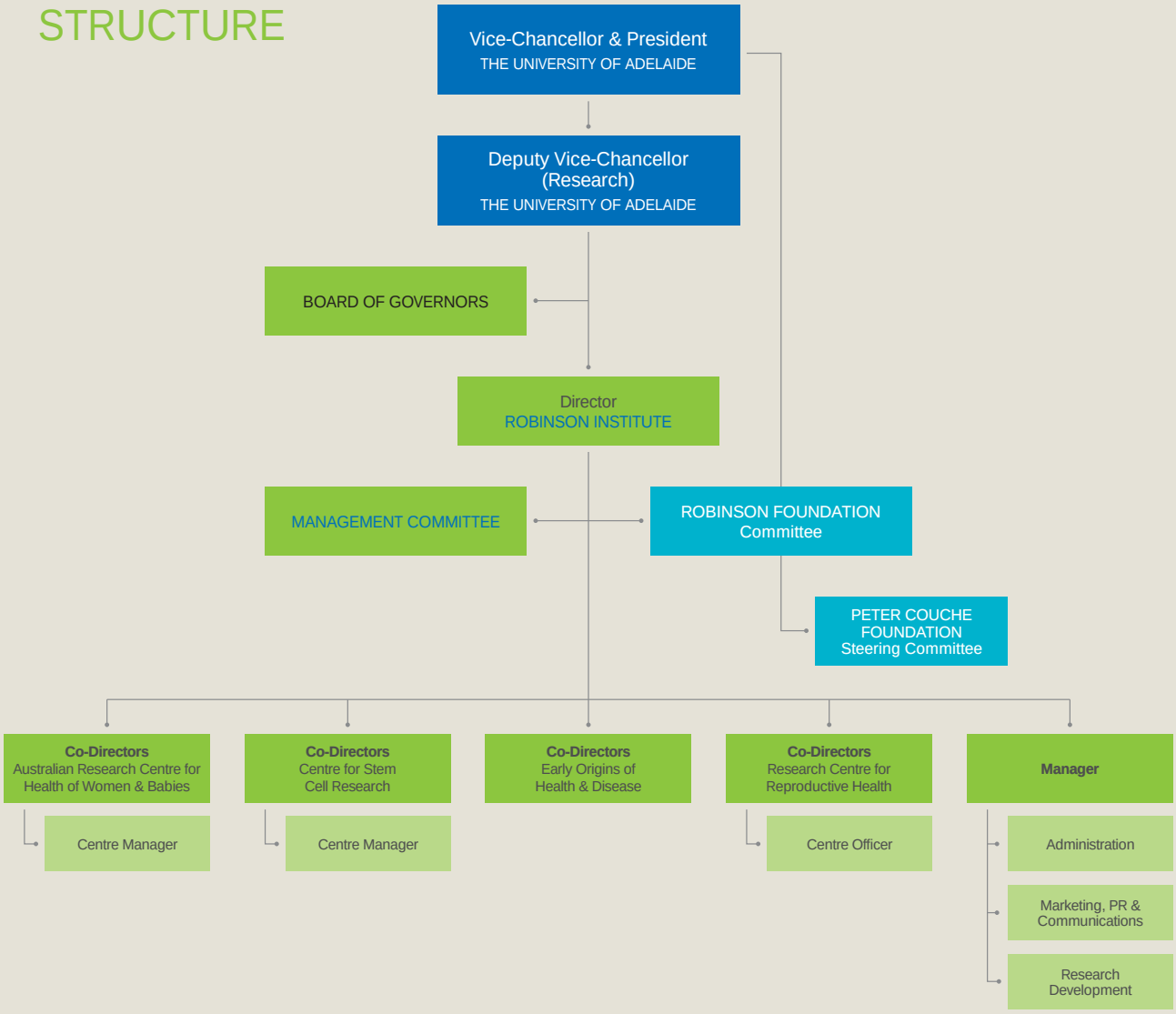
Equipment is an important part of these upgrades and goes hand in hand with dedicated expertise. We are establishing and rationalising new core facilities that will centralise and build our platform capabilities. This ensures we keep up with the latest technologies and provide our researchers with access to both the equipment and the support they require to productively carry out their research.

An example of such a facility is our Gene Silencing and Sequencing Facility, which will be fully functional in 2011. We have been fortunate in employing an excellent scientist, Dr Darren Miller, to set up and manage this facility, who will provide invaluable advice and assistance to many of our research groups.

We are ambitious in our aims to acquire and maintain cutting-edge facilities, but it truly will deliver the best research results and we are confident that with government and community support we can have a thriving research facility here in South Australia.

(from left) Joanna Close, Jackson Jaensch, Imogen Craig & Alissa Nightingale

STRUCTURE

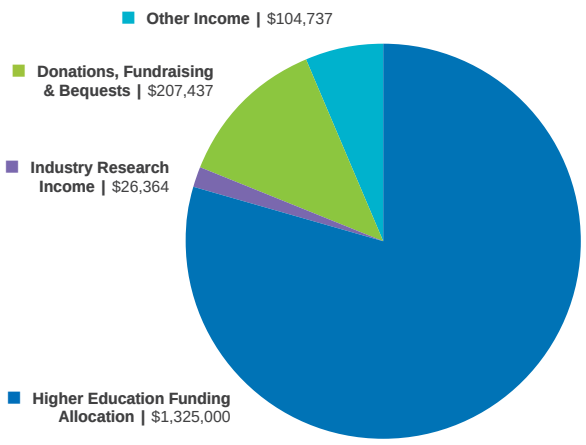


FINANCIALS

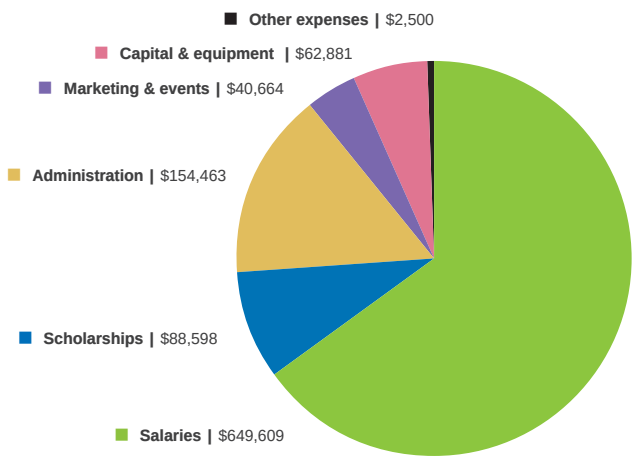
The financials presented in the illustrations below provide details for the Robinson Institute department only, and therefore exclude research income earned directly by members. Further information on income of our members can be found on page 22.

Net Operating Result | $664,823

Revenue | $1,663,538



Expenditure | $998,715



COMMERCIAL DEVELOPMENT

In 2010, 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. There is further strong commercial engagement with many researchers in the Robinson Institute.

IVF breakthrough

Professor Sarah Robertson has partnered with a Danish company to develop a product which improves IVF embryo implantation rates. In the world's largest clinical trial on IVF media, Professor Robertson and Origio a/s – a European company specialising in assisted reproductive technologies – have shown for the first time that growth factor molecules are critical to ensuring optimal embryo development. The resulting product, EmbryoGen, to be released in 2011, contains a signalling molecule called GM-CSF found naturally in the mother's tissues which protects the embryo from stress, making it stronger and more robust in the early implantation period. The product is mainly effective in women who have previously miscarried, where an impressive 40% increase in implantation success was shown.

Development of diagnostic tests for pregnancy complications

As part of the SCOPE (Screening for Obstetrics & Pregnancy End Points) Program, Institute researchers Professor Gus Dekker and Professor Claire Roberts have formed several commercial development collaborations with Mosaiques Diagnostics GMBH, Alere and Pronota, with the intention to develop and commercialise diagnostic tests to predict pregnancy complications such as preeclampsia, preterm birth, gestational diabetes and fetal growth restriction.

Embryo selection technology for IVF

Dr Darryl Russell and Ms Kathryn Gebhardt have developed an embryo selection test designed to identify IVF embryos which have the best developmental potential. This technology was protected by a provisional patent and a development relationship was established with an IVF provider to validate the technology in the commercial IVF setting.

IVF Vet Solutions

The IVF Vet Solutions business unit, led by Associate Professor Jeremy Thompson, provides various services to the IVF market, including the mouse embryo assay (MEA), which is a quality assurance test for media and other products used in IVF. The unit is also developing a suite of bovine IVF media, supported by Adelaide Research & Innovation's Commercial Accelerator Scheme. Under the development program, IVF Vet Solutions is producing and supplying research media to collaborating commercial bovine IVF providers, with the goal of validating the media suite in a commercial setting.

Expert panel to the NHMRC

The Institute's Australian Research Centre for Health of Women and Babies (ARCH) team was appointed to an NHMRC Panel of Providers with Expertise Relevant to the Development and Presentation of Evidence Based Health Advice. ARCH is developing dietary guidelines for pregnant and breastfeeding women and is providing support on obesity guidelines.

Collaboration with Cook Medical to improve in vitro maturation of oocytes in humans

A collaborative relationship is ongoing between Associate Professor Jeremy Thompson, Dr Robert Gilchrist and Cook Medical on technologies to improve the in vitro maturation of oocytes in humans.

In 2010 the Robinson Institute also worked with Cook Medical on establishing the Cook Medical Adelaide Fellowship. This Fellowship will provide the opportunity for

Dr Wendy Ingman

new collaborations between Australia and the People's Republic of China. Through the Fellowship we hope to develop prominent young researchers in Australia and China by exposing them to a new research environment and to open the door to potential new and long-term collaborations.

Production and supply of antibodies

Associate Professor David Kennaway has a commercial relationship with Buhlmann Laboratories involving the supply and use of melatonin antibodies.

Clinical trials

Various Robinson Institute researchers are conducting sponsored clinical trials with companies such as Bayer, Abbott Cardiovascular and Merck Serono Australia.

IVF media additive to improve implantation and placentation

A collaborative developmental program investigating the use of IGF-II to improve implantation and placentation is ongoing between Professor Claire Roberts and Origio a/s.

SUPPORTING OUR RESEARCHERS

In 2010 the Robinson Institute offered research support to sustain and establish a number of research programs and projects and to develop our students and researchers.

The Robinson Institute sees an internally directed research support program as an initiative that can both encourage current members in developing a higher level of research quality and productivity, as well as attracting the next generation of researchers.

Internal funding programs enable our members to diversify their portfolio of funding sources and may encourage specific programs and styles of research, as well as facilitating new research initiatives and collaborative projects. Our support has also proven crucial in establishing a number of the Institute's higher risk or early stage projects that would not necessarily be able to obtain Commonwealth funding.

A number of internal funding schemes were offered to Robinson Institute members in 2010:

- The New Directions Funding Scheme, a new initiative in 2010, provided seed funding for applications to alternative external funding bodies, and supported its five recipients by facilitating ample preparation, planning and review. A requirement of the scheme was that applications be submitted by an early or mid career researcher, to encourage the active participation of these individuals in grant proposal preparation. Up to $15,000 was offered to each group across two application stages.
- Another new program in 2010, the Collaborative Research Program, began with two Research Leader Discussion Forums, where the research focus, capabilities and potential of a number of research groups were presented by research leaders to their peers. The Collaborative Research Funding Sheme followed, funding project applications from teams made up of Robinson Institute members from across different research groups and centres. Apart from facilitating these collaborations, the purpose of this program was to drive the development of new and highly competitive research projects that answer major research questions. Six teams were awarded funding of between $10,000 and $12,000.

New Directions Funding Scheme

Dr Annette Osei-Kumah & A/Prof Vicki Clifton EOHaD | $15,000

Dr Emily Steele & A/Prof Vivienne Moore EOHaD | $14,946.60

Dr Julia Pitcher & A/Prof Michael Ridding EOHaD | $13,842

Dr Rosalie Grivell, Dr Lisa Moran & Prof Jodie Dodd ARCH | $15,000

Dr Tamara Varcoe & A/Prof David Kennaway RCRH | $14,315

Collaborative Research Scheme

A/Prof David Kennaway, Dr Rebecca Robker & Dr Darryl Russel RCRH | $12,097

A/Prof Michael Davies, A/Prof Leonie Heilbronn, Prof Robert Norman & Prof Julie Owens EOHaD & RCRH | $10,000

A/Prof Michael Davies & Dr Catherine Gibson EOHaD & ARCH | $10,000

A/Prof Simon Koblar & A/Prof Michael Ridding EOHaD & CSCR | $12,000

Dr Claire Jessup, A/Prof Toby Coates & Dr Claudine Bonder CSCR | $12,000

Dr Wendy Ingman, Dr Carmela Ricciardelli, Dr Darryl Russel & Dr David Sharkey EOHaD | $12,000

CASE STUDY

STIMULATING THE BRAIN TO MAKE STEM CELL THERAPY A SUCCESS

Associate Professor Simon Koblar and Associate Professor Mike Ridding have teamed up under the Robinson Institute's Collaborative Research Program to determine a technique that will promote the success rate of newly emerging stem cell therapies for stroke repair.

Stem cell therapy is perhaps one of the most promising approaches being developed to treat stroke, the nation's second greatest killer. However, there are currently a number of limitations with such techniques. Some of these limitations could be overcome by providing a more supportive environment within the brain to promote stem cell survival and facilitate appropriate connectivity. Simon, with his background in stroke and stem cell work, and Mike, with expertise in magnetic brain stimulation (a technique normally used to assess brain plasticity and not as a therapy in itself), will assess whether non-invasive brain stimulation techniques could in fact be used to enhance the local brain environment for stem cell implants.

The Robinson Institute's Collaborative Funding Scheme has enabled this pilot study, which may lead to a significant breakthrough in the success rate of future stem cell therapies for stroke repair.

Lisa Akison

Professional development and mentoring

Professional development became a focus of the Robinson Institute in 2010 through the launch of two internally run programs.

A Mentoring Program saw the Institute's seven Honours Scholarship holders each paired with a PhD student or early career researcher. The program intended to build interactions and support networks across the Institute by facilitating a relationship that would not otherwise be formed. By matching individuals from different laboratories, both mentor and mentee were provided with the opportunity to openly discuss not only research-related issues but also personal, relational and career development topics.

The Robinson Institute's Personal Growth Program began in the second half of 2010, with monthly half-day sessions focusing on soft skills for researchers. Sessions were run by senior research staff as well as externally sourced professionals, with topics across the year including:

- Personality profiling
- Intellectual property
- Science communication and public speaking
- Leadership and team dynamics
- CV development.

Scholarships

In 2010 the Robinson Institute offered scholarships to honours and postgraduate students:

- Scholarships were awarded to five students undertaking their PhD within the Institute. These awards offered students $5,000 per year over the three years of their full-time postgraduate degree.
- Seven Honours Scholarships were funded, with the purpose of attracting high quality undergraduate students to the research programs of the Institute and to support them in their transition from undergraduate coursework to research. The Jeffrey Robinson Honours Scholarship awarded $7,000 to the highest scoring student, with a further six scholarships awarding $4,000 each.
- Additionally, two Honours Scholarships of $3,000 each were offered under the separately funded Bradley Norman Honours Scholarship scheme.

Postgraduate Scholarships

Jessica Laurence RCRH
$15,000 over 3 years

Joanna Cole EOHaD
$15,000 over 3 years

Mitchell Goldsworthy EOHaD
$15,000 over 3 years

Saidatul Mohammad EOHaD
$15,000 over 3 years

Shanshan Han ARCH
$15,000 over 3 years

Honours Scholarships

Lauren Sandeman CSCR | $7,000

Candice Houda EOHaD | $4,000

Chin Ng RCRH | $4,000

Kisha Sivanathan CSCR | $4,000

Nigel Farrow CSCR | $4,000

Sowmya Cheruvu RCRH | $4,000

Wing Ng RCRH | $4,000

Bradley Norman Honours Scholarship

Ryan Rose RCRH | $3,000

Georgia Martin RCRH | $3,000

CASE STUDY

BRADLEY NORMAN HONOURS SCHOLARSHIP

In 2006 the Research Centre for Reproductive Health (now a centre of the Robinson Institute) was approached by Mr Robert and Mrs Wendy Norman, who were grieving the loss of their only son Bradley who had tragically passed away at the age of 19. Bradley had been conceived through IVF, and at his funeral Mr and Mrs Norman requested donations be made in order that a scholarship be set up to support young students within the field of assisted fertility treatment.

The Bradley Norman Honours Scholarship was awarded to its first recipient in 2007 and has supported a number of honours students since.

In 2010, scholarships of $3,000 were awarded to Georgia Martin and Ryan Rose, who undertook honours within the Institute's Oocyte Biology Laboratory.

Georgia's project focused on purifying and comparing two forms of oocyte-specific growth proteins to determine one that could potentially be used to enhance reproductive technologies. Ryan undertook a project that investigated a new approach to in vitro maturation (IVM) technology to increase success rates.

CASE STUDY

DRIVEN TO FIND A CURE FOR CYSTIC FIBROSIS

Following the diagnosis of his daughter Ella with cystic fibrosis, Nigel Farrow was driven to a career in medical science to work towards a cure for this debilitating disease.

At the age of 39, Nigel left his career in music and enrolled in a medical science degree at the University of Adelaide. Nigel joined the Robinson Institute in 2010 after receiving an Honours Scholarship from the Institute to investigate innovative approaches for cystic fibrosis treatment using stem cells.

Cystic fibrosis is the most common inherited genetic condition affecting young Australians, with a child being born with the disease every four days. Currently, over 3,000 children and young adults in Australia are living with the condition.

It is caused by a mutation in the gene that regulates sweat, digestive juices, and mucus in the lungs. Repeated infections and blockages can cause irreversible lung damage and death. Mucus can also cause problems in the pancreas, preventing the release of enzymes needed for the digestion of food.

The aim of Nigel's research is to use a modified virus to "carry" the therapeutic or "wanted" gene into the body to reach airway stem cells.

The gene's characteristics would then be passed on to those stem cells, producing the correct daughter cells to improve lung function and provide a better quality of life for cystic fibrosis patients.

Nigel says that this research provides an "entirely new way to do medicine. But more research needs to be conducted to be completely sure that it works and is safe to eventually give to children born with cystic fibrosis."

Nigel has recently been awarded an MS McLeod PhD Scholarship worth $75,000 to continue his quest for a cure.

He will use this funding over a three-year period to investigate ways of correcting the cellular defects that cause cystic fibrosis, particularly looking at the role of stem cells in the respiratory pathway in sustained corrective gene expression.

Nigel Farrow and his daughter Ella

RESEARCH HIGHLIGHTS

Funding success

In 2010 Robinson Institute members received over $16.3 million in income, primarily from Commonwealth funding schemes. Projects included the following:

- Professor Julie Owens (Head of the School of Paediatrics and Reproductive Health, and Robinson Institute Research Centre Director) was awarded the University of Adelaide's largest single grant in 2010 from the NHMRC of $891,732 for a project investigating the link between growth-restricted babies and diabetes and obesity in later life.
- Professor Caroline Crowther (Centre Director, ARCH) received $1.08 million from the NHMRC for two individual projects: $632,979 to investigate whether the right diet and lifestyle can help treat borderline gestational diabetes in pregnant women; and $447,281 to review the link between corticosteroids and improved health in preterm babies.
- Associate Professor Simon Koblar (Centre for Stem Cell Research and School of Medicine) received $590,048 from the NHMRC for a project to understand the role of a gene his group has discovered in repairing the brain after stroke.
- Associate Professor Frank Grutzner (Research Centre for Reproductive Health) was awarded $710,000 from the ARC for a study of the evolution and function of sex chromosomes and genes in mammalian reproduction.

Publications

2010 was a successful year for the Robinson Institute, with over 300 papers by Institute members published during the 12 months. Of particular note were a number of articles published in the high ERA and impact factor ranking journals, Journal of Obstetrics and Gynaecology, and a paper published in the high profile journal Nature. A total of 23% of Robinson Institute publications were in journals ranked as A* under ERA rankings, with another 30% in A-ranked journals.

ERA results

The Excellence in Research for Australia (ERA) initiative was introduced in 2010 as a Government-administered process to assess the research quality at universities across Australia. Under the research area of paediatrics and reproductive medicine, the University of Adelaide was the only university in Australia to achieve a maximum score of 5, ranking it highest in the nation. The score ranks this research area well above world standard, confirming that the Robinson Institute and the School of Paediatrics and Reproductive Medicine has established a foundation for current and continuing world-class research.

Dr Lisa Moran (L) & Dr Claudine Bonder

2010 Research Fellowships:

Dr Louise Hull | $493,695 (over 5 years)
SA Health Mid Career Practitioner Fellowship

Michael O'Callaghan | $23,500
Endeavour Research Fellowship

A/Prof Michael Davies | $785,232
ARC Future Fellowship

Prof Ray Rodgers | $765,370
NHMRC Research Fellowship

Dr Wendy Ingman | $600,000
National Breast Cancer Foundation Early Career Fellowship

Dr Natasha Rogers | $372,528
NHMRC Training Fellowship

Jacqueline Boyle | $320,032
NHMRC Training Fellowship

Dr Amanda Highet | $290,032
NHMRC Training Fellowship

Dr Sebastian Doeltgen | $290,032
NHMRC Training Fellowship

Dr Nicolette Hodyl | $290,032
NHMRC Training Fellowship

Dr Dominic Wilkinson | $245,022
NHMRC Training Fellowship

New Senior Researchers

Associate Professor Leonie Heilbronn

Associate Professor Leonie Heilbronn completed her undergraduate degree at the University of Adelaide, and then honours and a PhD at CSIRO where she examined the effects of different dietary fats during weight loss and the genetics of obesity.

After several postdoctoral years spent in a world-class obesity centre in the USA and at the Garvan Institute in Sydney, Leonie returned to Adelaide in 2010 to take up an appointment as a Research Leader within the Robinson Institute's Research Centre for Reproductive Health. Her research lies mainly in the field of obesity and type 2 diabetes mellitus with a focus on understanding the molecular and physiological basis of obesity and its associated diseases in humans.

CASE STUDY

BRAIN GENE A TRIGGER FOR DETERMINING GENDER

Above: Associate Professor Paul Thomas

Researchers are a step closer to unravelling the mysteries of human sexual development; following genetic studies that show male mice can be created without a Y chromosome - through the activation of an ancient brain gene.

Males usually have one Y chromosome and one X chromosome, while females have two X chromosomes. A single gene on the Y, called SRY, triggers testes development in the early embryo, and once these begin to form, the rest of the embryo also becomes male.

However, researchers have discovered a way of creating a male mouse without a Y chromosome by activating a single gene, called SOX3, in the developing fetus. SOX3 is known to be important for brain development but has not previously been shown to be capable of triggering the male pathway.

In a major international collaborative study, they also have shown for the first time that changes in the human version of the same gene are present in some patients with disorders of sexual development. The results of this work are published in the Journal of Clinical Investigation.

“The Y chromosome contains a gene called SRY that functions as a genetic switch to activate the male pathway during embryonic development,” says Associate Professor Paul Thomas.

“The SRY genetic switch is unique to mammals and is thought to have evolved from the SOX3 gene during early mammalian evolution.”

Associate Professor Thomas and his colleagues have generated male mice with two X chromosomes by artificially activating the SOX3 gene in the developing gonads. “These XX male ‘sex reversed’ mice are completely male in appearance, reproductive structures and behaviour, but are sterile due to an inability to produce sperm,” he says.

“We have suspected for a long time that SOX3 is the evolutionary precursor gene for SRY. By showing that SOX3 can activate the male pathway in the same way as SRY, we now believe this to be true.”

This work is a **longstanding collaboration between Associate Professor Thomas and Dr Robin Lovell-Badge at the National Institute for Medical Research in London**, who discovered the SRY gene in mice more than 20 years ago. Dr Lovell-Badge says he’s excited about the findings: “SOX3 normally functions in the development of the nervous system, but it is now clear that a mutation that makes it active in the early gonad can turn it into the switch that makes testes develop.

“It is now very likely that something similar to what has happened in the XX male mice and humans we describe also occurred in our early mammalian ancestors, and this led to the evolution not only of SRY, but of the X and Y chromosomes. Just think of all the trouble this little gene has caused!” he says.

Further collaborative research with Professor Andrew Sinclair at the Murdoch Children’s Research Institute in Melbourne and Professor Eric Vilain at UCLA (University of California Los Angeles) has also shown that changes in the human SOX3 gene are present in some individuals who are XX males.

“From a genetic perspective, cases of XX male sex reversal are particularly intriguing and are poorly understood,” Associate Professor Thomas says.

“This discovery provides new insight into the genetic causes of disorders of sexual development, which are relatively common in the community.

“For the future, this discovery will impact on the molecular diagnosis of these disorders and, ultimately, help us to develop therapies or technologies to improve clinical outcomes,” he says.

Associate Professor Thomas is a research leader with the Institute’s Centre for Stem Cell Research.

Dr Lisa Moran

Dr Lisa Moran has a background in molecular biology, physiology and a professional qualification as a dietician, and undertook a PhD focusing on the dietary management of polycystic ovary syndrome (PCOS) through the University of Adelaide and CSIRO. This includes work with the award-winning CSIRO Total Wellbeing Diet Research Team. In 2008 she was awarded an NHMRC Postdoctoral Fellowship for the Jean Hailes Foundation Research Group at Monash University. Lisa took up the opportunity to return to Adelaide in 2010 to continue her fellowship within the Robinson Institute.

Her current research focus includes the assessment and treatment of reproductive and metabolic features of polycystic ovary syndrome and the development of optimal preconception lifestyle interventions.

Dr Claudine Bonder

Dr Claudine Bonder completed a PhD at Flinders University and a postdoctoral position at the University of Calgary (Canada), through which she gained expert experience in cellular biology, inflammation, and the study of the immune system.

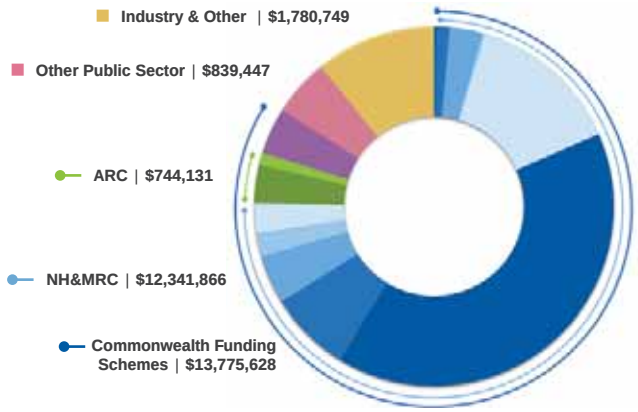
Since 2005 Claudine has worked within the Vascular Biology Laboratory within IMVS (now SA Pathology), which became a group of the Centre for Stem Cell Research within the Robinson Institute in late 2010. Claudine's research interests focus on understanding the role endothelial progenitor cell differentiation and the trafficking and activation of the blood vessels in an organ or tissue during normal and disease states (such as autoimmune disease, cancer, or acute and chronic inflammation).

Awards

Researchers from the Robinson Institute were recognised for their important contribution to research and the community through a number of awards including:

- Professor Alastair MacLennan
  Appointed an Officer of the Order of Australia
- Dr Natasha Rogers
  Ross Wishart Memorial Award (from the Australian Society for Medical Research), President's Prize for the Best Research Presentation at the annual meeting of the Australian and New Zealand Society of Transplantation, and the National Winner of the AusBiotech-GSK Student Excellence Award
- Dr Kylie Dunning
  South Australian Young Investigator Award and Research Trainee Award at the Society for the Study of Reproduction Conference
- Dr Alice Rumbold Future Justice Prize
- Dr Leonie Heilbronn
  SA Young Tall Poppy of Science
- Peter Couche
  Pride of Australia Award for Courage
- Professor Claire Roberts Robinson Institute Director's Award
- Dr Prabha Andraweera
  Zuspan Award – Best Young Investigator – Basic Science at the International Society for the Study of Hypertension in Pregnancy (ISSHP) Conference
- Dr Nicolette Hodyl
  Australasian Epidemiological Association Price for first place in Postgraduate Epidemiology Course
- Dr Lachlan Moldenhauer
  Young Investigator Award at the International Congress of Reproductive Immunology (ICRI) Conference
- Ashleigh Smith
  Young Investigator Award at the International Congress of Clinical Neurophysiology.

2010 | Member Income $16,395,825



COMMONWEALTH FUNDING SCHEMES

National Health & Medical Research Council	
NHMRC Australia Fellowships	$36,254
NHMRC Career Development Awards	$192,080
NHMRC Centres for Clinical Research Excellence	$488,125
NHMRC Development Grants	$37,429
NHMRC Program Grants	$2,262,803
NHMRC Project Grant	$6,617,650
NHMRC Research Fellowship	$1,204,681
NHMRC Research Support Grants	$720,552
NHMRC Training Fellowships	$351,913
Other NHMRC Funding	$430,380
Total National Health & Medical Research Council	$12,341,866

Australian Research Council	
ARC Discovery Project Grants	$565,421
ARC Future Fellowships	$178,710
Total Australian Research Council	$744,131

Other Commonwealth Funding Schemes	839,447.00
TOTAL COMMONWEALTH FUNDING SCHEMES	**$13,775,628**
Other Public Sector	$839,447
Industry & Other	$1,780,749
TOTAL MEMBER INCOME	**$16,395,825**

CASE STUDY

PROFESSOR ALASTAIR MACLENNAN APPOINTED OFFICER OF THE ORDER OF AUSTRALIA.

Professor Alastair MacLennan was appointed an Officer of the Order of Australia for his 40 years' work in women's and children's health, in particular unravelling the causes of cerebral palsy. Professor MacLennan has conducted feto-maternal research since 1970 and is the author of 340 refereed publications, books and scientific chapters.

The 2009 South Australian Scientist of the Year for Public Good has an international reputation for leading the world's largest research group into the causes of cerebral palsy, which affects more than 30,000 people in Australia.

Professor MacLennan and his team of researchers have recruited thousands of Australian families to provide cheek swabs and blood samples to help unravel the mystery of how genetic mutations are linked to cerebral palsy. The study is the largest of its kind in the world and seeks to find genetic answers to a disability that affects the neuro-motor region of the brain at birth, resulting in poor muscle coordination and even quadriplegia.

Apart from his reputation as one of the world's foremost cerebral palsy researchers, Professor MacLennan is also an international expert on menopause and women's health. He has received millions of dollars in Federal Government health funding for his research into both cerebral palsy and the role of hormone replacement therapy in treating menopausal symptoms.

Professor Mike Brooks, Deputy Vice-Chancellor and Vice-President Research at the University of Adelaide, says the Australia Day honour conferred on Professor MacLennan is "highly deserved recognition for a lifetime body of work".

"Professor MacLennan has spent more than 40 years improving the standards of obstetrics and gynaecology around the world. **In that time he has made significant breakthroughs in helping to pinpoint the causes of cerebral palsy**, as well as making an outstanding contribution to women's health."

Professor Alastair MacLennan

CASE STUDY

DEVELOPING MATERNAL FETAL MEDICINE IN INDONESIA.

Robinson Institute researchers have helped to establish a program that will see Indonesian maternal medicine trainees rotate through Adelaide in the final year of their traineeship.

In 2010, Robinson Institute affiliate member Associate Professor John Svigos secured AusAID funding that will support three Indonesian maternal fetal medicine trainees to spend eight weeks in the Women's and Children's and the Lyell McEwin Hospitals, observing consultations with outpatients, attending intervention sessions and participating in clinical and postgraduate education meetings. John will take up the role of overall coordinator of the rotation, while Institute members Dr Rosalie Grivell, Professor Gus Dekker and Professor Alastair MacLennan have assumed other key roles in the program. These include assistance with establishing the Indonesian trainee program through running training workshops for supervisors back in Indonesia and coordinating trainee placements at the respective South Australian hospitals when trainees come out in October 2011.

Trainees come from a consortium of three maternal fetal medicine divisions in Indonesian hospitals in Bali province and East Java, which members and affiliates of the Robinson Institute are currently working with. The significance and potential of such a rotational scheme is reflected in Indonesia's current, alarming maternal mortality rate of 340 deaths per 100,000 live births and perinatal mortality rate of 50–100 deaths per 1,000 live births (compared with Australia's rates of 6 and 8, respectively).

Currently, maternal fetal medicine trainees in this part of Indonesia have limited opportunity to gain overseas experience. The additional training will provide skills that will allow them to assist in addressing the maternal and perinatal mortality for women and their babies in Indonesia.

The Indonesia rotational scheme will enable these trainees to become far more informed about international health practice and policy. This will, in turn, raise their expectations of the Indonesian Government and health bodies, and thus help them to develop the capacity to act as informed advocates for their patients.

We are committed to translating research discoveries to improve clinical practice

CLINICAL AND RESEARCH TRIALS

The Robinson Institute's clinical and research trial facilities continued to develop in 2010. The Institute has dedicated facilities at our headquarters in North Adelaide, but we also conduct trials within some of South Australia's leading hospitals, including the Women's and Children's Hospital, Lyell McEwin Hospital and The Queen Elizabeth Hospital.

In particular, the Institute's Australian Research Centre for Health of Women and Babies (ARCH) continues to conduct significant clinical trials and studies. The appropriate evaluation of healthcare interventions by high quality randomised trials is absolutely essential to find out which treatments are most effective in different situations and for which individuals. The results from randomised trials provide people with the best evidence about healthcare options to inform recommendations for clinical practice and for further research.

Research is carried out within clearly identified priority areas. Currently ARCH conducts clincial trials and studies that include:

- Interventions to improve the health outcomes of infants born preterm
- Care for women with borderline gestational diabetes
- Prevention of preeclampsia
- Prevention of preterm birth
- Complementary and alternative medicine in women's health and during pregnancy and childbirth
- Support for women in pregnancy who are overweight or obese
- Management of the induction of labour
- Care for women after a previous caesarean section
- Surgical techniques at caesarean section
- Care of women with a multiple pregnancy
- Impact of health and care in pregnancy and childbirth and later maternal and child health.

The Institute received valuable support from local media to promote our research and recruit participants for our trials. Two particular studies that were promoted included looking at the links between heart disease and polycystic ovary syndrome, and another to develop diagnostics to predict adverse pregnancy outcomes.

CASE STUDY

PCOS AND LINKS TO HEART DISEASE

Robinson Institute researchers have found evidence of a link between a common hormonal disorder in women and heart disease. Polycystic ovary syndrome (PCOS) is a hormonal disorder affecting about 10% of women of reproductive age and is a leading cause of infertility.

A preliminary study – conducted by researchers with the Institute and the Cardiology Department of The Queen Elizabeth Hospital – has exposed other major health risks and some common misconceptions about PCOS.

The pilot study, involving a small sample of women, showed that:

- Young women (average age of 31 years) with PCOS had significant abnormalities in blood clotting and blood vessel function, which are important risk factors in heart disease;
- This risk was not limited to overweight or obese women with PCOS – it affected women of all body shapes and sizes, including lean women.

"The degree of blood clotting and blood vessel abnormalities seen in women with PCOS in this study was very striking, similar to what we would normally see in older patients with known heart disease," says Dr Alicia Chan, Cardiologist at The Queen Elizabeth Hospital and PhD student with the Institute. "With women now making up almost half of all Australians affected by heart disease, it's very important that we understand the link between PCOS and these heart disease risk factors.

"Importantly, this is the first study to suggest that PCOS is strongly associated with an increased risk of heart disease independent of women's weight or evidence of diabetes. It's a common misconception that only overweight or obese women are affected by PCOS – we need women to understand that they could still have these heart disease risk factors regardless of their weight," Alicia says.

In 2011, researchers will enter the next phase of the study and are recruiting more PCOS individuals to participate in the intervention strategies.

CASE STUDY

PREDICTING ADVERSE PREGNANCY OUTCOMES (PAPO)

A diagnostic test is being developed by the Robinson Institute that will identify couples at high risk of pregnancy problems, helping to **alleviate complications that occur in 20% of first pregnancies**.

The study sought couples planning to become pregnant, or those less than 12 weeks pregnant. Couples in the study underwent a blood test checking their folate, vitamin B and D levels, hormonal levels and immune system and completed a dietary and medical health questionnaire. The researchers also examined any genes associated with blood clotting, which are known to cause pregnancy complications.

“The most common difficulties are miscarriage, preeclampsia (high blood pressure in pregnancy) and preterm births. At present there is no way to predict which couples will develop these pregnancy problems,” Dr Denise Furness says.

All of these problems can threaten the life of both mother and baby. Preterm births alone can cost the healthcare system up to $5,000 a day for neonatal intensive care, and if a baby is born three months early it is a huge cost to the community, not to mention the parents’ emotional wellbeing.

The expected outcomes of the research are to be able to come up with diagnostics and tools to predict which couples are at risk of developing these adverse pregnancy outcomes.

“By learning more about risk factors we can help prevent and treat these problems for future pregnant women and their babies,” Denise says.

The PAPO study is coordinated through the Robinson Institute’s clincial trial facilities at the Women’s and Children’s and the Lyell McEwin Hospitals.

Dr Denise Furness

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.

Within the University of Adelaide, the Institute has strong collaborations with the School of Paediatrics and Reproductive Health, the Faculty of Health Science, and the Faculty of Sciences. Furthermore, the Institute has numerous collaborations with external educational and research institutions both in Australia and internationally. Other key partners of the Robinson Institute include:

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 and Hanson Institute

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

Children's Research Centre

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 illness before it manifests 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 impairments. It also pioneers interventions for sleep, gut, mental health, neurological and immune disorders, and studies the safety of new and existing vaccines.

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 Professor Robert Norman (Director of the Robinson Institute), Professor Caroline McMillen (University of South Australia) and Professor 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 in these areas.

Jean Hailes Foundation for Women's Health

The Institute collaborates with the Jean Hailes Foundation for Women's Health through the establishment of the National Alliance on Polycystic Ovarian Syndrome (PCOS). 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.

Institute for Photonics and Advanced Sensing

In 2010, the Robinson Institute began collaborating with the University of Adelaide's Institute for Photonics and Advanced Sensing (IPAS) to develop new technologies to advance reproductive health research and practice. This followed a successful grant from the Premier's Science and Research Fund from the South Australian Government of $700,000.

Fertility clinics

Researchers of the Robinson Institute are involved in the clinical practice and research development of two leading fertility clinics in Adelaide, Fertility SA and Repromed.

Women's and 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 Hospital 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.

CASE STUDY

UTILISING FIBRE OPTICS FOR NEW REPRODUCTIVE HEALTH TECHNOLOGIES.

Two leading University of Adelaide scientists, Professor Robert Norman (Director of the Robinson Institute) and Professor Tanya Monro (Director of the Institute for Photonics and Advanced Sensing), were awarded a $700,000 Premier's Science and Research Fund Grant from the South Australian Government to develop sensing technologies for advanced reproductive research.

Through this funding a collaborative transdiciplinary laboratory will be established that will lead the world in creating unique technologies for biomedical sensing and promote dialogue between two highly innovative disciplines.

This will enable South Australia's reproductive health researchers and clinicians to lead in adopting emerging optical fibre-based technologies, and seed the development of a new biotechnology industry for South Australia.

The majority of women experience some form of reproductive disorder over the course of their life, and many chronic and severe reproductive disorders remain without preventive strategies, clear diagnostics or successful treatment. Preventable reproductive disease costs Australia more than $3 billion per year and affects more than 25% of women between 15 and 45 years of age.

In addition, reproductive efficiency and pregnancy loss is a major issue in livestock breeding, directly impacting on other industries such as agriculture. However, at present it is not possible to monitor developing embryos or assess the uterine environment non-destructively.

In the 21st century, the greatest health gains stand to be made from research addressing the multiple points of vulnerability throughout the pre-birth and post-birth phases of life that are susceptible to the impact of internal and external influences. The very earliest stages of embryogenesis are the most susceptible.

These emerging sensing platforms will provide a richer understanding of the science of early embryo development, as well as improved diagnostics for endometriosis, reproductive cancers and infertility.

Professor Rob Norman and Professor Tanya Monro (courtesy The Australian)

ROBINSON INSTITUTE ANNUAL CELEBRATION

The Robinson Institute took the opportunity to unite and recognise our achievements over the past two years by holding a celebration on Monday 25 October. Over 100 people attended the event held at the University of Adelaide's new Innova21 Building.

Professor Jeffrey Robinson, Professor Robert Norman (Director) and Mr Ian Nightingale (Chair, Robinson Foundation) gave an overview of the significant research milestones and achievements made since our establishment, and of the exciting years ahead for the Robinson Institute.

The day also marked a milestone for our honours students who submitted their theses.

At the event, Professor Robert Norman awarded Professor Claire Roberts with the inaugural Director's Award. This award recognised Claire's embodiment of the values of the Institute, including her commitment to quality research; engaging and educating the community; providing a dynamic research environment; and providing mentoring for early career researchers.

Congratulations Claire!

Professor Claire Roberts


Research

ROBINSON FOUNDATION

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

- Raising vital funds required to seed 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 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 Foundation was officially launched in February 2010 at a gala dinner in the grounds of Government House. This event introduced over 250 people to the research of the Institute and marked the first fundraising initiative for the Foundation.

During 2010 the Foundation focused on formalising our structure within the University of Adelaide, developing fundraising and community engagement strategies, and growing our enthusiastic and committed Board.

The Institute and Foundation participated in a number of events during 2010 to raise awareness and further engage with the general public.

The Foundation was fortunate to be supported by the National Wine Centre through their fortnightly “Uncorked” program, with Tim Adams Wines in November and the Christmas event in December, where the Robinson Foundation received part of the proceeds of each glass and bottle of wine purchased.

Our researchers also presented at a number of events to showcase the research being conducted at the Institute and to educate the community about the health outcomes from our research. These included Professor Alastair MacLennan and Dr Kylie Dunning presenting to two Rotary groups; a Friends and Benefactors presentation in collaboration with the University’s Development & Alumni department; and Associate Professor Vicki Clifton giving a University of Adelaide Research Tuesdays Presentation.

By the end of 2010, the Robinson Foundation had accumulated $207,000 from fundraising activities, donations and bequests. A significant proportion of this sum, over $150,000, was raised by the Peter Couche Foundation, which sits within the Robinson Foundation.

The Foundation is grateful for the significant support received from the community to date. Our generous donors for 2010 are recognised on page 85.

In 2011, the Foundation will make its first call for applications for funding from researchers of the Institute. We look forward to reporting back to our supporters on the outcomes of this investment in research.

His Excellency, Governor of South Australia tours the Medical School

His Excellency Rear Admiral Kevin Scarce AC CSC RANR, Governor of South Australia, toured the Robinson Institute’s research facilities at the University of Adelaide’s Medical School in October 2010.

His Excellency viewed first-hand the research being conducted around pregnancy risks and complications, fertility preservation for female cancer patients, reproductive health and immunology, and new advances being made with stem cells.

His Excellency is joint patron of the Robinson Foundation with Mrs Liz Scarce.

PETER COUCHE FOUNDATION

The Peter Couche Foundation operates within the Robinson Institute at the University of Adelaide and raises awareness and important funds to support innovative research being conducted at the Institute using non-embryonic stem cells from teeth (known as dental pulp stem cells) to treat the effects of stroke.

Associate Professor Simon Koblar, one of Australia's leading stroke physicians, leads this research and believes stem cell research has great potential to unlock the mysteries of stroke damage and help restore brain function to improve the quality of life of stroke sufferers.

Research to date has indicated that these stem cells have an intrinsic ability to produce neurons (brain cells) and make a range of growth factors that are likely to help repair the brain. Some of these initial pilot studies were funded by a generous grant awarded by the Catholic Archdiocese of Sydney.

The significance of this research and the Peter Couche Foundation can be highlighted through the following facts:

- In Australia every 10 minutes someone has a stroke.
- Over 250,000 live with the aftermath of a stroke, making it the leading cause of disability in Australia.
- Stroke is Australia's second single greatest killer after coronary heart disease, and kills more women than breast cancer.
- Strokes cost Australia an estimated $2.14 billion a year.

And sadly, stroke could happen to any of us – just like it happened to Peter Couche, as a healthy, outgoing 41-year-old businessman on a trip through Singapore.

Peter's stroke occurred 20 years ago and he has since lived with "locked-in syndrome" – Peter's brain is as sharp and active as ever, but he has virtually no physical abilities.

Through the establishment of the Foundation, Peter aims to:

- Raise important funds needed to progress this stem cell research for brain repair in stroke victims
- Dispel the myths surrounding stem cell therapy
- Show the hope that is being generated through innovative research on non-embryonic stem cells
- Raise awareness of stroke, particularly that useful life does not end because someone has suffered a stroke.

In 2010, Peter was awarded the Pride of Australia Medal for Courage. This medal recognised his determination and strength of character to overcome personal adversity and is a well-deserved recognition for a truly inspirational man.

Peter Couche Foundation fundraising 2010

The challenge to improve brain function after a stroke is enormous and, like all research, what can be achieved depends on funds raised. In the year since establishment, the Peter Couche Foundation has raised over $150,000 to support this research and aims to raise $1 million over the next three years to determine if clinical trials in humans are a possibility for stroke victims using adult stem cells.

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

Peter Couche Foundation Committee

Mr Dom Cosentino
Mr Peter Couche
Mrs Simona Couche
Mr Stephen Couche, Chair
Mr Colin Dunsford
Mr Andrew Gerlach
Mr Stephen Gerlach
Mr Stephen Officer
Mr Mick Scammell
Ms Lisa Taplin

Above: A/Prof Simon Koblar, Simona Couche, Stephen Couche, Peter Couche, Professor James McWha & His Excellency Rear Admiral Kevin Scarce, Governor of South Australia

FUTURE

What's in store for the future of the Robinson Institute?

The Robinson Institute will continue to focus on undertaking high quality research – research that stands up to scrutiny in the international arena and delivers new discoveries that transform the lives of everyday people. We have excellent people and a worthy purpose, but we will need to make some big decisions about where the Robinson Institute will head in the future.

Australia is likely to be facing significant cuts in Federal Government funding for research. This is a major threat to our research programs and our researchers. The salaries of our researchers are funded through these Commonwealth programs, as are our equipment and our consumables. Without funding, our research will disappear.

So, there will be a number of ways that we attempt to tackle this issue…

Outstanding research profile: Keeping focused on the best research

We are focused on undertaking the best research, that will make a difference not only in South Australia but in the world. We have big aims for our research, including:

- Ensuring every family has the best chance to conceive a child
- Making sure every baby is born with the very best start to life
- Finding cures through the use of stem cells for diseases that currently offer little or no treatment.

We will continue to ensure that as a team we work collaboratively in the areas where we can have most impact. Our structure and our operations must support our efforts.

Dynamic working environment: Ensuring greatest efficiencies

We need to ensure that the funding we receive makes the biggest impact, and we can achieve this by continuing to gain greater efficiencies and leverage resources across our organisation. This may be as simple as better coordinating our equipment and expertise, streamlining administrative processes and ensuring professional development programs are in place to enhance productivity.

Quality researchers and students: Supporting our best researchers

Investing in our research leaders and their teams is incredibly important. We need to provide them with the tools to do the best job possible as efficiently as possible. The Robinson Institute will be investing in professional development programs to achieve this, including:

- Mentoring across the organisation: our key research leaders will be engaged with professionals to develop their personal skills; our early career researchers will be mentored by our leaders
- Programs to enhance publication productivity: making sure our researchers are equipped to get the needed results and work as a team to deliver findings across the globe
- Travel programs: to enable our researchers to travel to conferences and to other international research organisations to gain skills and knowledge that they can bring back to the Institute and share
- Technique workshops: sharing and leveraging the skills across our multidisciplinary teams.

Strong funding base: Diversifying our funding, relying on the support of our community

Increasingly we realise the need to diversify our funding base in order to sustain our research programs. We need to trust and rely on support from alternative funding organisations, from relevant foundations and trusts, and from the community. We will continue to increase our engagement with the community to gain their support and to deliver results to meet their needs.

Our research impacts this community by saving and improving lives – our work is a partnership.

Lauren Sandeman

Our research impacts this community by saving and improving lives – our work is a partnership.

AUSTRALIAN RESEARCH CENTRE FOR HEALTH OF WOMEN AND BABIES

CENTRE DIRECTORS' REPORT

All six research divisions within the **Australian Research Centre for Health of Women and Babies (ARCH)** have been highly productive in 2010, with eight new grants awarded, nine significant awards and scholarships received, and 80 publications recorded. Just over half of papers were published in A* ERA (Excellence in Research for Australia) journals.

The research divisions of ARCH are Research Synthesis, Clinical Studies and Trials, Indigenous Maternal and Perinatal Health, International Maternal and Perinatal Health, Translational Research and Research Networks and Education.

Guided by our strategic initiatives, ARCH research leaders and staff provide extensive expertise in research design, maternal and perinatal care, study coordination, psychological assessment, data management, statistics, research synthesis and knowledge translation. The effective partnerships within and between the ARCH research divisions in the Robinson Institute are highly valued, as are the significant achievements of individual staff and students.

Through its individual studies, collaborative research networks and educational programs, ARCH 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, New Zealand and internationally.

As ARCH strives to achieve better health through excellence in leadership, research, education and knowledge translation, we are making meaningful differences for women and babies and their families.

Director: Professor Caroline Crowther

Co-Directors: Professor Jodie Dodd and Ms Philippa Middleton

RESEARCH DIVISIONS

Research Synthesis

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

The Research Synthesis Division focuses on 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 Research Synthesis Division is a member of the Cochrane Collaboration, an international organisation committed to providing high quality, independent evidence to inform health care decision-making. Cochrane reviews combine results of the world's best medical research studies, and are recognised as the gold standard in evidence-based health care. Cochrane reviews in maternal and perinatal health have major impact by providing evidence for clinical practice and health care policy, and for identifying new research strategies.

The Australian Collaborative Research Network (the Cochrane Pregnancy and Childbirth Australian Review Authors Group) is funded by the Federal Department of Health and Ageing, with the national coordinating centre at ARCH.

Our Australian review authors contributed to 89 out of 324 (28%) of all the pregnancy and childbirth reviews, and 26 out of 101 (26%) of the protocols published in the Cochrane Library (as of Issue 12, 2010). Over the past year, members of the Cochrane Pregnancy and Childbirth Australian Review Authors Group were involved in preparing 12 titles, 12 protocols, 20 new reviews and 12 updated reviews, considerably exceeding our key performance indicators.

The Division actively monitors 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 provide intensive support to most protocols, reviews and updates being prepared for publication.

Funding was obtained from the NHMRC to conduct an individual patient data (IPD) meta-analysis on the use of repeat dose(s) of prenatal corticosteroids prior to preterm birth. The study will involve 11 international trial groups and aims to clarify which women and babies will benefit most from repeat corticosteroids and what is the optimal drug regimen. The international collaboration will be known as the PRECISE Collaboration (Prenatal REpeat Corticosteroid International IPD Study group: assessing the effects using the best level of Evidence).

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, A/Professor Dominic Wilkinson, Dr Andrew McPhee, Dr Chad Andersen

The Clinical Studies and Trials Division conducts 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, childbirth, infancy and later life – of relevance to women and babies worldwide.

ARCTURUS: Australasian Randomised Collaborative Trials Uniquely aRe US

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 unclear whether the benefits of similar treatment for women with more borderline gestational glucose intolerance outweigh any harm. The aim of this randomised clinical trial is 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.

The IDEAL trial received NHMRC Project Grant funding for 2011–14 of $632,979.

PPROMT: *Preterm prelabour rupture of membranes close to term*

This large, multinational 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.

The PPROMT trial received further Project Grant funding of $832,928 from NHRMC to be able to complete the study for 2011–13.

New research initiatives for 2010

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

MAGENTA: *Magnesium sulphate at 30 to 34 weeks' gestational age: neuroprotection trial*

Babies born very preterm have a greater risk of significant morbidities, including neurologic impairments such as cerebral palsy. The risk of morbidity increases with decreasing gestational age at birth. The Cochrane review evaluating the effect of magnesium sulphate on neuroprotection of the fetus shows that magnesium sulphate given to women at risk of imminent preterm birth reduces the risk of cerebral palsy. It remains unclear at which gestational age treatment will be beneficial. The National Clinical Practice Guidelines on Antenatal magnesium sulphate prior to preterm birth for neuroprotection of the fetus, infant and child recommends further randomised trials at 30 weeks' gestation or more. This had led to the MAGENTA study.

Seven ongoing major trials/studies coordinated by ARCH

Our seven ongoing major research studies are evaluating care during pregnancy and childbirth, care around preterm birth, and care for women with a multiple pregnancy.

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 and betamethasone, when 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 aim of this randomised trial is 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 2010.

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 complications, which may result in the need for early birth and rarely mortality. More recently, reports have emerged about utilising Doppler ultrasound to measure the fetal middle cerebral artery (MCA) peak systolic velocity (PSV) to determine the presence of fetal anaemia. Systematic review of the literature has indicated a lack of information from randomised controlled trials comparing this technique with standard measures based on prediction in the rate of fall in the fetal haemoglobin. Cohort studies reporting the use of fetal MCA PSV in this setting yield conflicting results. Clearly, high quality trials are a priority to assess the role of MCA PSV in determining the timing of second and subsequent fetal intrauterine blood transfusions, and the impact this has on fetal and neonatal morbidity, when compared with current standard care. The aim of this trial is to assess in the fetus, where one intrauterine fetal transfusion has been performed for anaemia due to red cell alloimmunisation, whether fetal MCA 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 childbirth 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 when using mobile phone technology for the reminders.

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 over 40% of pregnant women being overweight or obese. There are well-documented risks associated with obesity during pregnancy and childbirth, such as maternal complications including hypertensive conditions and preeclampsia, gestational diabetes, infection, thromboembolic events, need for induction of labour, caesarean section and perinatal death. Infants of mothers who are overweight or obese are more likely to be macrosomic, require admission to the neonatal intensive care unit, be born preterm, be identified with a congenital anomaly, and require treatment for jaundice or hypoglycaemia. The aim of this randomised controlled trial is to assess whether the implementation of a package of dietary and lifestyle advice to overweight and

obese pregnant women to restrict weight gain during pregnancy is effective in improving maternal and infant health outcomes.

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. Among 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 are 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 and has now completed recruitment. The results will be presented at the Perinatal Society of Australia and New Zealand (PSANZ) meeting in 2011.

CLOSURE: *Skin and subcutaneous fascia closure at caesarean section: a randomised controlled trial*

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.

CASE STUDY

LIMITING THE EFFECT OF OBESITY ON PREGNANCY

Research Leaders within ARCH have been conducting a study seeking to improve health outcomes in pregnancy by limiting weight gain in overweight and obese expectant mothers.

Obesity is a health issue that affects around 35% of women aged between 25 and 35 years during pregnancy and childbirth. The risks associated with obesity during pregnancy and childbirth are clear and these include high blood pressure and preeclampsia, gestational diabetes, infection, blood clots, the need for labour to be induced, the need for caesarean section, and perinatal death.

Infants of mothers who are overweight or obese are more likely to be macrosomic (have an excessive birth weight), require admission to the neonatal intensive care unit, be born preterm, have a congenital disorder, and require treatment for jaundice or hypoglycaemia.

Professor Jodie Dodd, Co-Director of ARCH says, “While there is much literature related to defining the problems and potential complications associated with obesity during pregnancy and childbirth, there is a lack of information available which relates to effective interventions to improve maternal, fetal and infant health outcomes.”

Expectant mothers involved in the LIMIT study participate in a comprehensive weight management plan that includes a combination of dietary, exercise and behavioural strategies in order to limit weight gain during their pregnancy.

Participants receive counselling from a research dietician on dietary advice following current Australian dietary standards, are provided with information about exercise during pregnancy, and are encouraged to make changes to their lifestyle. All this is designed to minimise participants’ weight gain during pregnancy to a maximum of 5 kg.

“The LIMIT study aims to assess whether a combination of dietary and lifestyle advice given to overweight and obese women during pregnancy in order to limit weight gain is effective in improving maternal, fetal and infant health outcomes,” says Professor Dodd.

Researchers within ARCH believe that dietary and lifestyle interventions are an effective way of improving health outcomes for mothers and babies. Researchers within the LIMIT study are striving to uncover treatments to reduce this major cause of maternal, infant and childhood morbidity.

STARS: Studies, Trials and Assessments after Research Studies

Cerebral palsy

The aim of the Cerebral Palsy Research Group is to determine whether cerebral palsy has a genetic basis and whether genetic susceptibility for cerebral palsy is triggered by environmental risk factors during pregnancy and early life.

The incidence of cerebral palsy in Australia, 2.5 cases in every 1000 births, has not changed in 50 years. This is despite a 6-fold increase in caesarean delivery which should have reduced cerebral palsy if the main assumed cause, problems in labour, was correct. It is now thought that probably less than 2% of cases are directly related to problems in labour.

The financial cost of cerebral palsy in Australia alone is over $5 billion per year. There is no cure for cerebral palsy and no proven method to prevent it. A better understanding of the causes of cerebral palsy is essential to allow preventive measures to be formulated and tested.

Led by Professor Alastair MacLennan, the South Australian Cerebral Palsy Research Group changed its name to the Australian Collaborative Cerebral Palsy Research Group when it set up the world's largest genetic and epidemiological study of cerebral palsy with collaborators throughout Australia. DNA was extracted from over 4,200 buccal swabs from case and control families throughout Australia. The study examined 35 candidate genes that may be associated with cerebral palsy through their influence on fetal or maternal inflammatory responses, thrombophilia or an increased risk of preterm labour. A large amount of epidemiological information was collected from state perinatal data sets, state cerebral palsy registers and maternal questionnaires. These data were linked to the genetic data. The results will be offered for publication in 2011.

This large Australian gene-association study of individual gene mutations has led in 2010 to an international collaboration with colleagues in the United States who have access to new second-generation genetic technology that allows much more detailed analyses of the human genome and the common variations of large submicroscopic segments of chromosomes that may predispose to neurological developmental disorders. These have been associated recently with autism, epilepsy and intellectual disability, but until now cerebral palsy has not been studied for these genetic variations. We are building up a large biobank of buccal and blood-derived DNA from cerebral palsy families to study potential genetic changes found by these increasingly sophisticated and expensive technologies, either through collaboration with our US collaborators or, if future funding permits, in Adelaide.

The three-year buccal swab DNA national study successfully finished recruitment in 2010, and all genetic and epidemiological data were entered into our databank for ongoing analyses. Scientific papers concerning these results are being prepared for submission for publication in 2011. Michael O'Callaghan, PhD student, has completed his thesis based on the gene-association study and, on behalf of the research group, published the study protocol and a systematic genetic literature review of this area. Gai McMichael started her master's thesis based on the new second-generation genetic methodologies, and has also published on improved methodology to extract viral DNA from stored neonatal blood spots. These data can also be linked with the same cases and controls.

Professor Alastair MacLennan and Matthew Reinertsen

CASE STUDY

MAGNESIUM SULPHATE PROTECTS BABIES AGAINST CEREBRAL PALSY

Despite recent advances in the care around the time of birth that have led to large increases in the survival rates for very preterm babies, the rate of adverse long-term neurologic problems has not diminished in survivors, and remains too high compared with children not born preterm.

Babies born preterm have a higher chance of dying in the first few weeks of life, and preterm infants who survive have greater risk of neurological impairments such as cerebral palsy, blindness, deafness, or cognitive dysfunction, and a greater risk of substantial disability as a result of these neurological impairments.

New National Clinical Practice Guidelines released by ARCH in 2010 have presented that giving pregnant mothers magnesium sulphate when they are at risk of very preterm birth (less than 30 weeks of gestation) can help protect their babies from cerebral palsy.

Preparation of the guidelines, Antenatal magnesium sulphate prior to preterm birth for neuroprotection of the fetus infant and child, was led by ARCH Director Professor Caroline Crowther, in collaboration with a number of representatives around Australia and New Zealand.

“For infants born very premature, there is a high risk of cerebral palsy,” says Professor Crowther. “These guidelines present evidence to support giving magnesium sulphate therapy to women at risk of very preterm birth to increase their unborn baby’s chance of survival, free of cerebral palsy.”

At present there is no cure for cerebral palsy, which makes effective preventive interventions of paramount importance.

Magnesium sulphate therapy involves giving doses of magnesium sulphate to pregnant women via injection. It is known that magnesium is vital for normal cell function, may protect against destructive molecules that can harm cells, and in some circumstances improves blood flow.

These guidelines have led to the development of the WISH project (Working to Improve Survival and Health for babies born very preterm), which will monitor and improve the uptake of antenatal magnesium for neuroprotection.

The group were fortunate to be granted funding from the Cerebral Palsy Alliance which will enable monitoring to improve the uptake of antenatal magnesium for neuroprotection in Australian tertiary maternity hospitals.

Full details of the guidelines can be downloaded at: www.adelaide.edu.au/arch.

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.

Three key multicentre trials, all funded by NHMRC Project Grants, are underway:

- ACTORDS 6–8 year follow-up: follow-up of children to early school age to assess the effect of repeat antenatal corticosteroids on childhood growth and development. The follow-up assessments will be completed in January 2011.
- MiG TOFU: follow-up of children at early school age to assess the effect of metformin on childhood development.
- LIMIT: follow-up of children at 6 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: Ms Philippa Middleton, Professor Caroline Crowther, E/Professor Jeffrey Robinson, Dr Alice Rumbold

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

ARCH continues to maintain and build its collaborations with Indigenous organisations, keeping up to date on current issues and policy changes, and seek collaborative funding opportunities where possible.

An affiliate group within ARCH has received NHMRC Project Grant funding to undertake a study entitled "Aboriginal Families Study: closing the gap in Indigenous maternal and child health outcomes".

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.

The SEA-URCHIN initiative (South East Asia – Using Research for Change in Hospital-acquired Infection in Neonates) received funding from the NHMRC for 2011–15 of $2,179,916. SEA-URCHIN will build on the successful SEA-ORCHID (South East Asia – Optimising Reproductive and Child Health In Developing Countries) Project that aimed to build capacity among health practitioners in evidence-based maternal and perinatal health in the developing countries that so badly need it.

SEA-ORCHID: Capacity building and evidence-based health care in South East Asia

The burden of mortality and morbidity related to pregnancy and childbirth remains concentrated in developing countries. SEA-ORCHID is evaluating whether a multifaceted intervention to strengthen capacity for research synthesis, evidence-based care and knowledge implementation improves adoption of best clinical practice recommendations, leading to better health for mothers and babies. In this study we assessed current practices in perinatal health care in four South East Asian countries and determined whether they were aligned with best practice recommendations.

We completed an audit of 9,550 medical records of women and their 9,665 infants at nine hospitals (two in each of Indonesia, Malaysia and the Philippines, and three in Thailand) in January–December 2005. We compared actual clinical practices with best practice recommendations selected from the Cochrane Library and the World Health Organisation (WHO) Reproductive Health Library.

We concluded that recording of clinical practices should be an essential step to improve quality of care. Based on these findings, the SEA-ORCHID project team has been developing and implementing interventions aimed at increasing compliance with evidence-based clinical practice recommendations to improve perinatal practice in South East Asia.

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.
- Provide support to the SEA-ORCHID project and similar initiatives.
- Encourage and support new maternal and perinatal research projects within South East Asia (SEA-URCHIN).
- Provide advice to the WHO projects on maternal and fetal health (Global Health Project on near-miss maternal mortality).
- Support development of the IMPAC (Integrated Management of Pregnancy and Childbirth) guidelines, 'Family and Community Health: Making Pregnancy Safer'

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.

The Division had a busy and exciting year in 2010, with the culmination of several projects and the beginning of new endeavours building on these projects. In 2010, NHMRC endorsed two of the clinical practice guidelines that ARCH developed or helped develop.

In February 2010, after a national competitive process, ARCH (specifically Philippa Middleton, Caroline Crowther and Vicki Flenady) was selected to be a member of NHMRC's panel of providers with expertise relevant to the development and presentation of evidence-based health advice. This enables ARCH to be considered for a range of national evidence-based health projects, particularly guideline development and updating.

ARCH has been at the forefront of national evidence-based guideline development and guideline methods during 2010.

- Perinatal Mental Health: As a member of the *beyondblue's* Guideline Expert Advisory Committee, Philippa Middleton helped to develop their perinatal mental health guidelines, *"Clinical practice guidelines for depression and related disorders (anxiety, bipolar disorder and puerperal psychosis) in the perinatal period"*, which were finalised in late 2010 and are now endorsed by NHMRC. These guidelines are intended for health professionals providing care in the perinatal period and are being implemented throughout Australia as an integral part of the Australian National Perinatal Depression Initiative.
- Antenatal Magnesium Sulphate: NHMRC endorsed *"Antenatal magnesium sulphate prior to preterm birth for neuroprotection of the fetus, infant and child: national clinical practice guidelines"* in November 2010. The development of these guidelines was led by ARCH (Caroline Crowther, Philippa Middleton, Tanya Bubner and Helena Oakey). A team from ARCH is currently working on ways to effectively implement the guidelines at local and national levels
- Dietary guidelines for pregnant and breastfeeding women: NHMRC has appointed a team consisting of Philippa Middleton (leader) and Caroline Crowther from ARCH, Carmel Collins, Maria Makrides and Jo Zhou from the Child

Nutrition Research Centre, Alice Rumbold, and Vicki Flenady from the Mater Medical Research Institute in Brisbane to prepare guidelines relating to outcomes for dietary intakes of mothers before and during pregnancy and while breastfeeding. This material is being integrated into the overall dietary guidelines for Australians. The draft documents will be released for public consultation in the first half of 2011.

- Other guideline development activity during 2010: Philippa Middleton led an update of the evidence for the NHMRC, *"Guidelines for the prevention of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to Australian hospitals"*, provided advice to the group producing the National Antenatal Care Guidelines, and was commissioned by the National Institute of Clinical Studies (NICS) to advise on scope and methods for developing national obesity guidelines.
- Formulating and grading guideline recommendations: The results of ongoing methodological work on designing the NHMRC system "FORM" for formulating and grading recommendations in evidence-based clinical guidelines has been accepted for publication in BMC Medical Research Methodology. The authors (Susan Hillier, Karen Grimmer-Somers, Tracy Merlin, Philippa Middleton, Janet Salisbury, Rebecca Tooher and Adele Weston) are a national team of method-ologists who provide advice to Australian guideline developers and NHMRC.

Stillbirth

Philippa Middleton has been working with Vicki Flenady and other colleagues on an international project researching the causes of stillbirth in high-income countries, synthesising the evidence for effective interventions to reduce the number of stillbirths, and determining stillbirth research priorities using group processes. Results of the overall project have been accepted by Lancet in the form of two articles as part of a special issue on stillbirth that will be published in early 2011.

New initiatives

WISH Project: Working to Improve Survival and Health for babies born very preterm

Once the antenatal magnesium sulphate guidelines were endorsed by NHMRC, published and disseminated, our attention has focused on addressing the implications of implementing these guidelines, since very few obstetric units are currently using magnesium sulphate for fetal, neonatal and infant neuroprotection.

Babies born early (less than 30 weeks of gestation) are at high risk of dying in the first weeks of life or later having cerebral palsy. New research evidence shows that giving mothers magnesium sulphate immediately prior to an early birth (at less than 30 weeks' gestation) significantly increases the chances of the baby surviving without cerebral palsy. The WISH Project aims to nationally monitor and improve the uptake use of antenatal magnesium sulphate as a neuroprotective therapy immediately prior to imminent (birth planned or definitely expected within 24 hours), early preterm birth (less than 30 weeks' gestation) to reduce the risk of the baby dying or having cerebral palsy. All tertiary maternity hospitals within Australia and New Zealand with a neonatal intensive care unit are being invited to take part and form the WISH Project Group. The Project will optimise the care of women at risk of imminent early preterm birth and so improve the chances of survival and long-term good health for their babies.

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. 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.
- Our 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.

Additional funding for 2010 was granted by the NHMRC to continue the WOMBAT Collaboration (WOMen and Babies' Health and Wellbeing: Action through Trials). This 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 oppor-tunities 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.

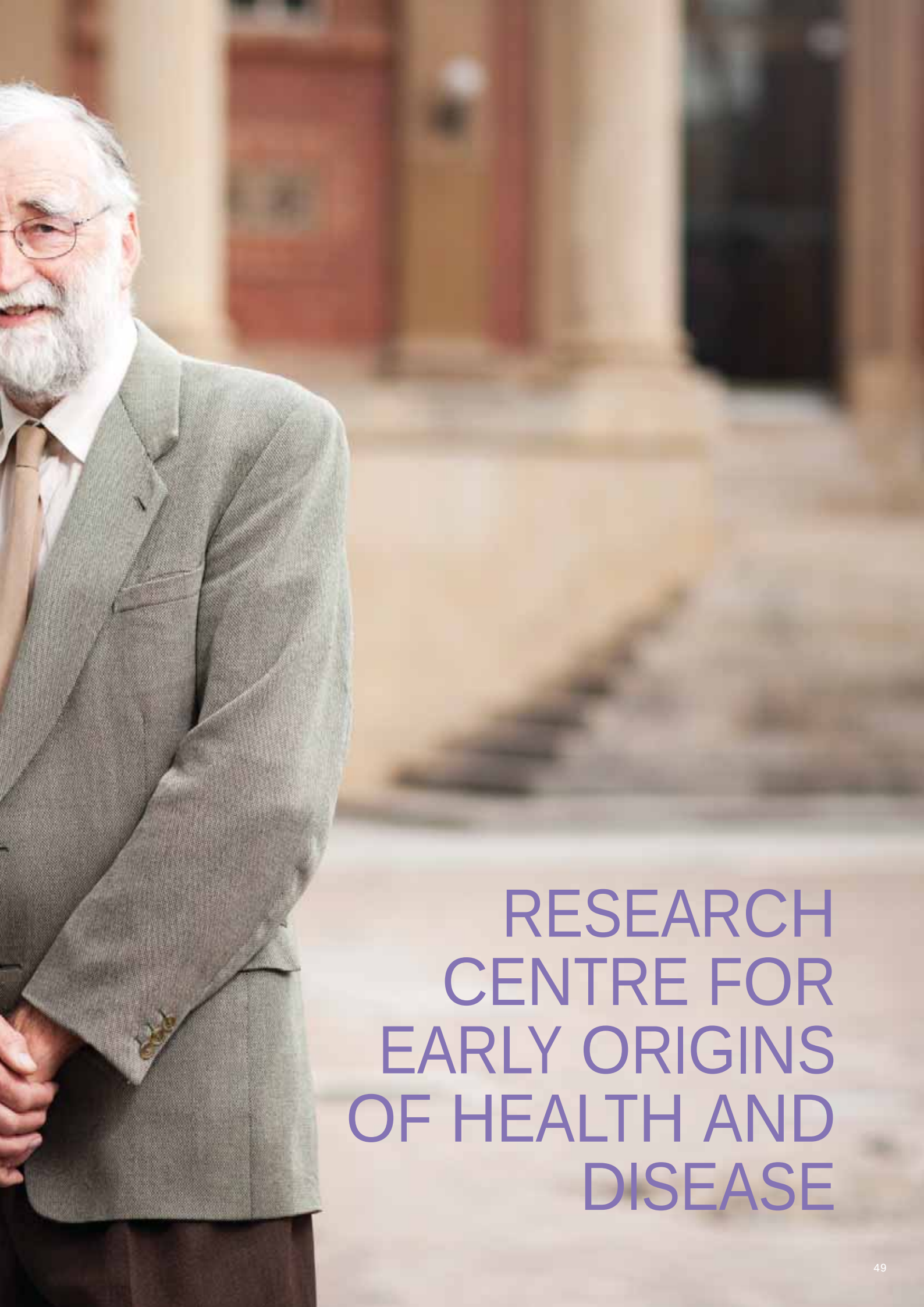
FUTURE

The future research initiatives of ARCH will continue to be guided by our strategic plan, and our commitment to excellence in conducting high quality, clinically relevant, maternal and perinatal research that will make a difference to the health of women and their babies.

We will continue to build on our areas of research strength and develop emerging areas of strategic importance through:

- Answering questions of major importance in the field of maternal and perinatal health, across the spectrum from preconception through pregnancy, childbirth, infancy and later life.
- Generating research evidence of the highest quality that promotes the best health possible for all women and their babies.
- Ensuring that research findings are incorporated into health care practice through the development of evidence-based practice guidelines and implementation research.
- Increasing capacity in research synthesis, randomised trials, and implementation and translational research through career development and education, locally, nationally, and internationally.
- Strengthening our existing collaborations and identifying new international, national and regional collaborations.

Professor Julie Owens and
Professor Jeffrey Robinson



RESEARCH CENTRE FOR EARLY ORIGINS OF HEALTH AND DISEASE

CENTRE DIRECTORS' REPORT

The Research Centre for Early Origins of Health and Disease (EOHaD) is a leader in the investigation of the intergenerational and perinatal origins of metabolic, cardiovascular, neurological and reproductive health in postnatal life. EOHaD includes four main research groups who have a research focus consistent with this general theme.

The Centre's membership spans disciplines from public health and epidemiology to molecular biology and epigenetics, and includes research groups at the University of Adelaide and their collaborators at external organisations in Australia and overseas.

Major activities revolve around defining how the early environment before and after birth affects development and health in childhood and later life, in four main areas:

- Early Origins of Health and Disease 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.
- Life Course and Intergenerational Health (LIGHt) focuses on understanding health and wellbeing across the genders and the reproductive life course; with the aim of identifying opportunities for the prevention of serious diseases among women and their children, it focuses on the social and biological pathways to health at different points in the life course.
- Neuromotor Plasticity and Development (NeuroPAD) involves researching the way that the brain, nerves and muscles create and control movement in the human body.
- Pregnancy and Development 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.

Directors:

Professor Julie Owens

Associate Professor Michael Davies

Associate Professor Michael Ridding

CASE STUDY

ENHANCING MEDICAL RESEARCH AT THE LYELL MCEWIN HOSPITAL

Professor James McWha, the Vice-Chancellor and President of the University of Adelaide, officially opened specialised wet laboratories at Adelaide's Lyell McEwin Hospital on Tuesday 30 March.

The site hosts the Robinson Institute's Pregnancy and Development Group led by Associate Professor Vicki Clifton. The redevelopment was significantly supported by the University of Adelaide's School of Paediatrics and Reproductive Health.

The research group focuses on the health of pregnant women and the growth of unborn babies, with ongoing work monitoring the health of the children throughout their lives.

The group has a particular interest around pregnant women with asthma, half of whom are likely to have an asthma attack during their pregnancy.

Research has shown that the human fetus is able to deliberately slow and modify its development in response to a suboptimal maternal environment, such as if the mother has a pre-existing disease or suffers extreme stress.This action increases its chances of survival. But remarkably, only female fetuses use the ability. Males instead "roll the dice" and attempt to continue growing at their normal rate, placing them at greater risk should further complications arise.

"What we hope to do is actually look at how we treat pregnant women, through understanding when their babies are at risk and when they are not. Asthma worsens in reproductive-aged women and just being pregnant can make women more susceptible to an asthma attack," says Associate Professor Vicki Clifton.

Vicki says many women with asthma are not being identified during pregnancy. "It's being under-reported during antenatal visits and therefore under-treated. There is also a misconception with pregnant women that their asthma medication may harm the baby. In fact, the asthma is much more likely to be harmful than the preventive medicine," she says.

She says that **55% of women with asthma will have at least one acute asthma attack during pregnancy** and that can lead to detrimental effects on the baby including growth restriction, preterm delivery or even stillbirth.

The research shows that if asthma is managed properly there is less risk of an acute attack and therefore reduced risk of poor outcomes for the baby.

In 2010, Vicki discussed this fascinating growth mechanism and its possible implications for managing pregnancy in a University of Adelaide Research Tuesdays presentation.

Associate Professor Vicki Clifton and Pratiti Nath (courtesy The Messenger)

RESEARCH GROUPS

Early Origins of Health and Disease

Research leader: Professor Julie Owens

The Early Origins of Health and Disease Group aims to understand how events in early life, and possibly in previous generations, affect our health and risk of major diseases, including diabetes and obesity; to delineate the mechanisms involved, including epigenetic pathways; and to design and test effective interventions.

The group utilises a range of experimental paradigms in non-human species to investigate early life programming of health and disease; to study its mechanistic basis down to the molecular level; and to test possible interventions. We are able to directly study the initiation and progression of programming before birth, and the long-term functional outcomes for metabolic control and the endocrine axes that regulate these.

Current research programs include: early life programming of diabetes and obesity by placental restriction of fetal growth, maternal obesity and paternal obesity; and micronutrient, dietary and other interventions in mother and offspring to overcome placental programming of metabolic disease, including folic acid and methyl nutrients, omega-3 fatty acids and GLP-1 agonists.

Research outcomes:

- Identification of the father as a novel source of developmental programming of metabolic health in offspring and a novel target for intervention.
- Chronic high-fat diet in fathers programs -cell dysfunction in female rat offspring. Published in Nature in conjunction with our collaborators, this is the first report that a paternal high-fat diet, obesity and diabetes impair glucose tolerance and insulin deficiency in offspring with epigenetic changes in islet molecular signature.
- First demonstration that placental programming of obesity and subsequent impaired insulin action, and diabetes involves early induction of increased feed intake and resistance to endogenous leptin in young offspring, in association with excess visceral adiposity.
- Placental restriction increases plasma leptin and alters its relationship to feeding activity in the young lamb.

Life Course and Intergenerational Health (LIGHt)

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

The overall aim of the LIGHt Group is to identify opportunities to improve health and prevent disease among women and their children, focusing on both social and biological pathways at different points in the life course.

Our 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 outcomes:

- First to demonstrate the effect of source, timing and dosage of folic acid supplementation in pregnancy on risk of asthma in the child. This research invites a shift in understanding of asthma aetiology.
- Conducted the largest community-based study of polycystic ovary syndrome (PCOS) prevalence. The study shows a substantial proportion of women with undiagnosed PCOS and sets the path for unravelling the causal paths to a major cause of infertility.
- A community-based study that quantified the extent of reproductive difficulties among young South Australian women. This is one of the few community-based studies to document infertility in women in their early thirties.

- Developed a paper that critically considers public health efforts to reduce child obesity and the way women are positioned in this debate.

Neuromotor Plasticity and Development (NeuroPad)

Research leaders: Associate Professor Michael Ridding and Dr Julia Pitcher

The NeuroPAD Group investigates the neurophysiological mechanisms underlying developmental, or acquired, brain dysfunction, in order to develop novel therapies aimed at reducing the often-profound impact of these impairments on quality of life at all ages.

Approximately 10% of all infants born in Australia each year are born preterm (less than 37 completed weeks of gestation) and research has shown that even mildly preterm birth and poor fetal growth alter normal brain development, affecting an individual's physical abilities, educational outcome and social adjustment.

There is increasing evidence that, compared with their term-born peers, these children have higher rates of infant illness; have a greater likelihood of rehospitalisation in childhood; experience motor, cognitive and

behavioral dysfunction at school age; have greater participation in special education programs; and, as adults, have a lower net income and reduced likelihood of completing a university education, even without evidence of an obvious disability.

Currently, NeuroPAD is one of only a few groups internationally researching the long-term neurodevelopmental and neurologic outcomes in these children and is developing therapeutic interventions to ameliorate their impact on life quality.

The team is internationally known for their research using transcranial magnetic brain stimulation (TMS) techniques, which allow non-invasive and painless investigation of neural function in specific cortical regions of the human brain.

Research outcomes:

- TMS was used extensively in a cohort of children to show that every week of gestation up to term (approximately 41 weeks) is important in normal brain development.
- Recently discovered that two short sessions of brain stimulation, separated by around 10 minutes, give a much more robust neuroplastic response than one session.
- In a world first, NeuroPAD's researchers have recently used these techniques in children and shown that, compared with their term-born peers, the cortex of children born preterm is much less responsive to neuroplasticity induction. By understanding the physiology underlying their common difficulties with learning and memory, we have a much better chance of developing effective intervention strategies to help these children reach their full potential.

Pregnancy and Development

Research leader:
Associate Professor Vicki Clifton

The growth of a fetus and the development of a child into an adult is a physiological wonder. The Pregnancy and Development Group is interested in how a fetus grows when the pregnancy conditions for growth are suboptimal, and why males and females are different in how they adapt to pregnancy.

Maternal asthma during pregnancy and preterm neonates are our two major research areas. Maternal asthma is the most prevalent disease to affect pregnancy in Australia and is associated with a number of poor outcomes for mother and baby, including preterm delivery. Maternal asthma is a serious complication as it contributes to 20% of all preterm births, 15% of all growth-restricted babies and 15% of all stillbirths in Australia.

Asthma and pregnancy research involves basic research examining mechanisms in the placenta and fetus that may contribute to sex-specific differences in the fetal response to asthma. Our work has shown that this disease is under-reported and under-managed during pregnancy, resulting in preventable poor outcomes for the fetus.

The work conducted in preterm neonates has a focus on examining the health of preterm neonates and under what conditions these babies develop life-threatening infections. Our research relates to the programming of the immune system and the impact of oxidative stress in utero which then alters susceptibility to infection in the neonatal intensive care unit (NICU). We propose that male and female neonates are programmed by different factors which increase their susceptibility to infection and therefore may require different treatments for their survival.

Research outcomes:

- Published two important, high impact factor articles on asthma during pregnancy. The first provided an important message for health professionals and pregnant mothers with asthma, as it shows that the use of inhaled corticosteroids does not affect the fetal markers of adrenal function. This suggests that these drugs do not cross the placenta and are not harmful to the baby. The second article has a more basic science focus and identified that cortisol effects on fetal growth are not mediated by changes in gene or protein expression of the glucocorticoid receptor. This is important in that it identifies alternative mechanisms aside from the glucocorticoid receptor that may contribute to the development of glucocorticoid resistance.
- Asthma SA, in collaboration with Asthma Australia, has decided to nationally promote awareness of the treatment of asthma during pregnancy to health professionals and pregnant women.
- Initiated an education program in collaboration with the disciplines of Anthropology and Media to improve the ways we communicate with pregnant women and their networks, with the aim of encouraging positive and healthy behaviour in pregnancy.
- Updated the guidelines for the treatment of asthma during pregnancy in the Asthma Management Handbook. Produced by the National Asthma Council Australia, the publication used by all clinical services in Australia.

FUTURE

The Research Centre for Early Origins of Health and Disease (EOHaD) will continue to build its research leadership internationally by developing major synergies across research groups in the Robinson Institute and leading groups around the world.

Key themes are; gene–environment interactions and social and epigenetic pathways in maternal and paternal programming of metabolic and the neurological health of offspring and interventions.

To promote such collaborations, EOHAD will support a number of targeted workshops to highlight and realise potential opportunities through collaboration, joint grant applications and co-supervision, and will build its national and international affiliate networks through exchanges of staff and students.

Equally, EOHAD is committed to the further scientific and professional development of its members. To this end, a number of initiatives are planned for 2011 and beyond, targeting our current identified needs in statistics, modelling and bioinformatics support.

CASE STUDY

JUSTICE PRIZE FOR INDIGENOUS HEALTH RESEARCH

Dr Alice Rumbold, a perinatal epidemiologist, received the national Future Justice Medal in 2010 for demonstrating leadership and initiative in Australia's most disadvantaged sector, particularly for her work helping Indigenous women to overcome life-threatening reproductive diseases.

For the past five years Alice has worked with Aboriginal and Torres Strait Islander communities, researching why Indigenous women are more susceptible to reproductive cancers and other health problems.

Alice said Indigenous people faced 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," Alice said. "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," she said.

Infant and maternal mortality are around 2.5 and 3 times higher for Indigenous women than for non-Indigenous women, and Indigenous children were also found to be:

- Around twice as likely to be born preterm or to have low birth weight
- More likely to suffer from infectious conditions, parasitic diseases, respiratory and circulatory diseases, ear health and hearing problems, dental conditions, injuries and conditions related to social and emotional wellbeing
- More likely to be hospitalised as a result of such issues.

Health issues such as low birth weight transcend the individual, impacting not only on the child's early survival but also on their risk of chronic disease late in life, resulting in intergenerational transmission of poor health. Many of these poor outcomes are a result of preventable risk factors, or lack of access to appropriate health care.

Having worked closely with these remote communities, Alice feels she has been privileged to gain an understanding about Indigenous cultures and she is committed to an ongoing process of learning about these cultures.

Her experiences and relationships with communities will continue to shape her research program, and help ensure that this research program is addressing the key reproductive health issues identified by Indigenous women.

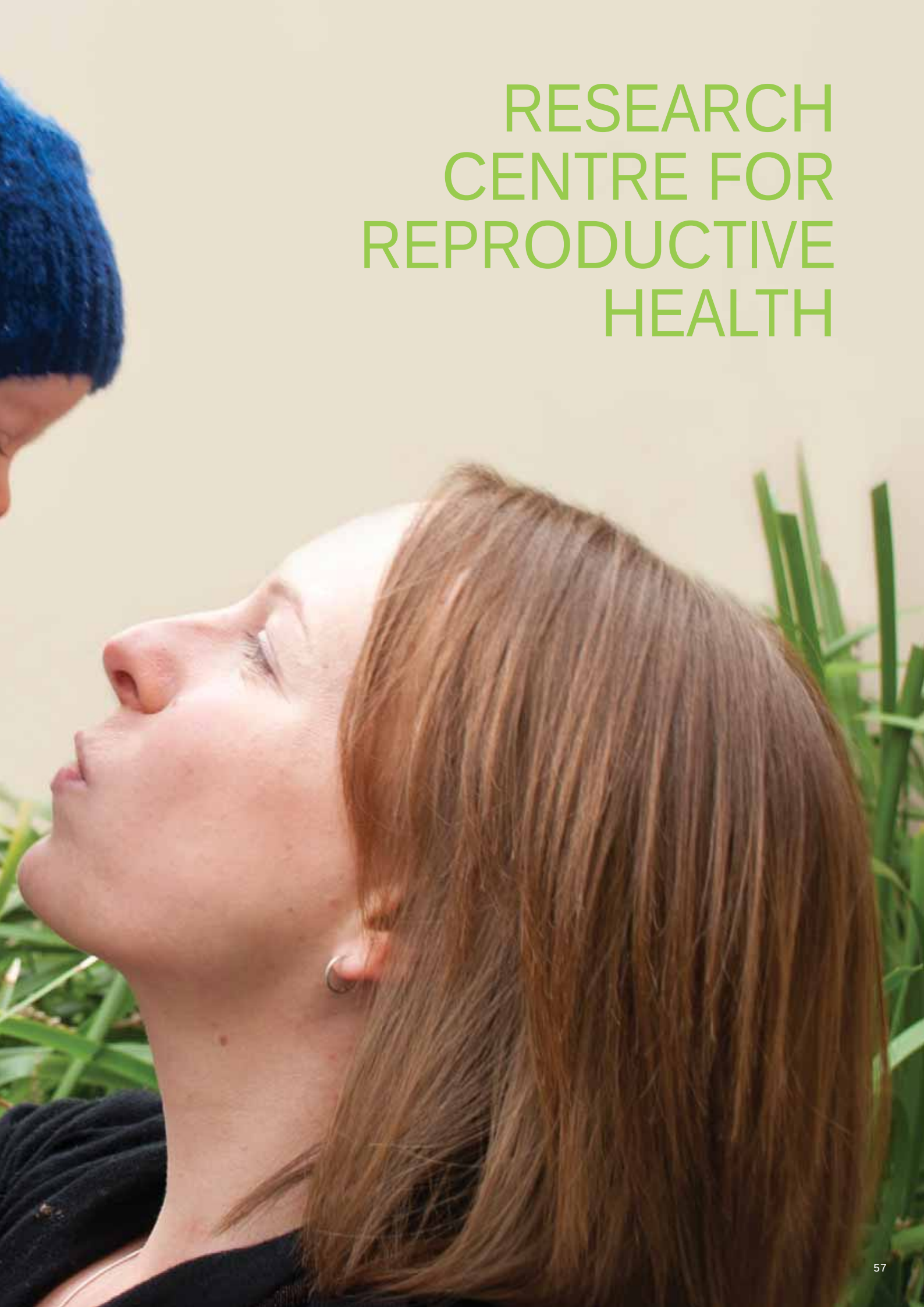
The Director of the Robinson Institute, Professor Rob Norman, said Alice demonstrated leadership and achievement "beyond her years as a researcher in a career that has demonstrated not only scientific excellence, but also a developing series of tangible outputs in the area of Indigenous health."

Alice is currently chief and associate investigator on several NHMRC grants that total more than $2.4 million and was South Australia's Young Tall Poppy of the Year for 2009.

Dr Alice Rumbold

Renee Cooper and son Alex (who was born at just 23 weeks)

RESEARCH CENTRE FOR REPRODUCTIVE HEALTH



CENTRE DIRECTORS' REPORT

The Research Centre for Reproductive Health focuses on achieving excellence in reproductive biology and medicine research. Our goal is to explore and advance the fundamental biology underlying the reproductive process, and to use that knowledge to improve reproductive health in women and men, and the health and resilience of their children. We achieve this through defining the most important and urgent research questions in reproductive medicine, accessing the most informative clinical tissues and model systems, and ensuring our research is well supported by cutting-edge biomedical research technologies.

The Centre's research spans ovarian biology and oocyte production, early embryo development, embryo implantation and placental development, seminal fluid and the male contribution to conception, as well as fetal development, birth, and mammary gland function. The impacts of intrinsic genetic, immune and infectious factors, and their interaction with external influences, including nutrition, stress and physiochemical and social environment, are of particular interest in our changing world.

Through understanding how tissues and processes operate under optimal and perturbed conditions, we unravel causal pathways involved in infertility and miscarriage, and pathologies of pregnancy including preeclampsia, fetal growth restriction and preterm delivery. Our discoveries are leading to improved methods for assisted reproduction and other novel treatments for infertility and subfertility, and also have applications in animal biotechnology and agriculture.

An important initiative in 2010 was the establishment of the GSEx core facility for gene silencing and expression, in line with our strategy to provide core facilities and invest in platform technologies that will expand research capability and facilitate first-rate research outcomes.

To ensure the clinical relevance and scientific rigour of our research, we foster collaborations between scientists and clinicians in reproductive medicine, obstetrics and gynaecology, endocrinology and cancer, and pursue industry outcomes through commercial partnerships. Additionally, we advocate linkages with government, health service providers and industry to maximise impact on reproductive health service and delivery.

Directors:

Professor Sarah Robertson

Associate Professor Jeremy Thompson

RESEARCH GROUPS

Circadian Physiology

Research leader:
Associate Professor David Kennaway

The Circadian Physiology Group is investigating the relationships between daily rhythmic changes in gene expression in various organs and physiological functions, and the consequences of disrupting the rhythmicity.

More than 17% of the Australian workforce is engaged in shiftwork and the work schedules disrupt hormonal and sleep rhythms, eating patterns and light exposure. There is strong emerging epidemiological evidence that shiftwork increases the risks of developing metabolic syndrome (obesity, insulin resistance and cardiovascular disease), as well as impairing fertility and increasing the risks of certain cancers (for example, breast cancer). An understanding of why this occurs will help us develop new strategies or drugs to reduce one of the important environmental triggers for poor health and impaired fertility.

Research outcomes:

- The group published a comprehensive study of the reproductive consequences of deletion of a critical clock gene called Bmal1 on reproductive function in female mice. This study showed that loss of function of this gene rendered the mice profoundly infertile and showed that the effects were multifactorial, impacting on the hypothalamus, pituitary and ovary.

Comparative Biology of Mammalian Sperm & Eggs

Research leader:
Associate Professor William G Breed

The Comparative Biology of Mammalian Sperm and Eggs Group carries out research on the coevolution of mammalian gametes (the sperm and eggs) and on the cellular and molecular processes that take place during sperm–egg interaction at the time of fertilisation. This is fundamental to the understanding of the continuity of life in mammals (including humans) and will provide insight into some of the underlying causes of infertility, and also form the basis for the development of species-specific based immunocontraceptive methods.

Our research uses a combination of microscopical and molecular techniques to determine the morphology of sperm and eggs, and the molecules involved in sperm–egg interaction at the time of fertilisation. We are also interested in environmental effects on reproduction, in particular those of high temperature and obesity.

Research outcomes:

In 2010 the group published five papers. Results include:

- A cellular study of the marsupial oviduct and, in particular, that of the glycoproteins produced that may bind to the sperm and/or recently ovulated oocyte and bring about the final gamete maturational events.
- Evidence for the evolution of marked diversity in sperm head form within a discrete group of mammals. Showed that the interspecies differences of head shape correlate with sperm tail length, suggesting a functional relationship between these two morphological parameters.
- Evidence that whole-body exposure to a hot environment results in a significant reduction in motility of much of the cauda epididymidal sperm population and that this is due to cell membrane damage. These effects eventually lead to germ cell apoptosis and hence a reduction in fertility – a problem that is going to become all the more important in the years to come due to global warming.

Early Development

Research leader:
Associate Professor Jeremy Thompson

The Early Development Group aims to provide infertile women with treatment options that achieve a safe and healthy pregnancy.

Our research focuses on understanding oocyte biology and very early developmental events. This primarily involves understanding the effect of so-called “energy sensing” signalling pathways in oocytes and early embryos, as these interpret the body’s metabolic state. Conditions such as obesity, diabetes and hypoxia all reduce oocyte and embryo developmental competence.

The group aims to provide safe, effective oocyte in vitro maturation procedures and to understand how diet and lifestyle choices affect oocyte quality, with the aim of developing new interventions that improve oocyte competency and early development.

Research outcomes:

- In collaboration with Dr Robert Gilchrist, a major clinical trial was established with Vrije Universiteit Brussel, Belgium, evaluating a new in vitro oocyte maturation system, which aims to advance a safer and more cost-effective infertility treatment. This is coupled with our continuing efforts to mimic the cAMP signalling events associated with the ovulatory stimulus.
- The group has identified several proteins of cumulus cell (nurse cells to the oocyte) that are altered in function under hyperglycaemia, which have significant effects on oocyte competence. In collaboration with Dr Karen Kind, we have also identified the role of hypoxia-signalling elements within cumulus cells and the oocyte, indicating that these are sensitive to hypoxia. We have also collaborated with Dr Kylie Dunning and Dr Rebecca Robker in determining that endogenous lipids within bovine oocytes are capable of providing most of the energy requirements for early development, but require the specific lipid metabolism cofactor carnitine to do so.

Gamete and Embryo Biology

Researcher leader: Dr Michelle Lane

The Gamete and Embryo Biology Group aims to solve questions that improve clinical practice in the area of reproductive health. This basic science research has direct impacts on clinical practice.

Reproductive health is affected by lifestyle and environment. However, the mechanism for these reductions in health is unknown and there are unanswered impacts on the health of the pregnancy and babies.

Infertility treatment is on the rise around the world. There are a number of lifestyle choices implicated in this increase, such as the decision to delay childbirth, and also factors such as obesity. Epidemiological data suggests that there is a relationship between many lifestyle factors and a decline in fertility; however, the direct mechanisms are unclear.

Research outcomes:

- Our group has been a leader in the concept that male obesity affects not only the quality of the sperm, but also the health of the resulting embryo and offspring. Our studies on both animal models and humans have established that having an obese father reduces fertilisation, and also results in poorer embryo development, reduced pregnancy rates and increases in pregnancy loss.
- The group has also determined that the outcomes of couples undergoing IVF are poorer if the male partner is obese.
- Understanding that the male partner can impact on the health of the pregnancy and also the health of the baby will result in a new clinical focus to male preconception health.

Genome Organisation, Epigenetics and Sex Determination

Research leader:
Associate Professor Frank Grutzner

The Genome Organisation, Epigenetics and Sex Determination Group is using a comparative genomic approach in distantly related mammalian species (platypus and echidna) to isolate and characterise new genes involved in normal and abnormal aspects of reproduction.

Disorders in human sex determination and differentiation are relatively common (approximately 1 in 100) and lead to a spectrum of abnormalities. The diagnosis of these malformations is complex and, in addition to the medical implications for the patient, has a huge social and psychological impact on parents and patient. Knowledge of the genes involved in sexual development is essential for diagnosis and for the efficient and targeted treatment of these developmental defects.

This research will provide new genes involved in sexual development in all mammals including humans, and also reveal new disease genes that will help to understand disorders in human sex determination and reproduction.

Research outcomes:

- Identified new genes on monotreme Y chromosomes that have potentially important roles in mammalian sex determination and placentation.
- Discovered that genes involved in the piRNA pathway that represses retrotransposon activity are expressed in the mammalian ovary and in ovarian cancer. This raises the possibility of this pathway having an important role in human folliculogenesis and ovarian cancer.

Growth Factors

Research leader: Dr David Mottershead

The Growth Factor Group aims to determine how the oocyte-secreted proteins, GDF9 and BMP15, function. These two proteins are essential for normal mammalian fertility, and they exhibit a unique synergism when added together to the cells that surround the oocyte. We believe understanding the mechanism of this synergism will enable us to help develop improved infertility options.

The proteins are structurally unique within the family of proteins to which they belong, and based on their structure we have hypothesised that they function as a complex. Hence, the major objective of the laboratory is to determine if this is the mechanism of their synergism. Our laboratory and our collaborators are the only investigators producing and purifying biologically active forms of these human proteins.

Research outcomes:

- The production and purification of the human oocyte proteins GDF9 and BMP15 from tissue culture cells.
- The demonstration that part of the structure of these proteins acts as an inhibitor or brake on the biological activity of the protein, and that this part needs to be removed for full bioactivity to be released.
- The demonstration that our purified human GDF9 and BMP15 proteins synergistically stimulate the growth of ovarian granulosa cells.

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 prenatal and postnatal development and health.

Programming of DNA via epigenetic modification, such as DNA methylation, is responsible for some effects on gene expression and phenotype. Prenatal epigenetic changes have effects on healthy development and disease throughout life. The group has a special interest in determining the effect of genetic differences on epigenetic programming and phenotype.

We use a worldwide unique intraspecies bovine hybrid model and resource collection of embryos and fetuses. This maximises heterozygosity and allows us to quantify differences in epigenetic modifications and mechanisms and their impact on embryonic, fetal and postnatal growth and development.

Research outcomes:

Major findings in 2010, by our group and with others, include the first description of:

- Extensive plasticity in imprinting of IGF2R in the placenta that could explain the seemingly contradictory data obtained in humans.
- Distinct patterns of gene-specific methylation in mammalian placentas and DNA methylation-mediated down-regulation of DNA methyltransferase-1 (DNMT1) in human placenta.
- Significantly increased variation in the epigenome of adult SCNT clones previously thought to have a normalised epigenome.

Mammary Gland Biology

Research leader: Dr Wendy Ingman

Currently, 1 in 9 Australian women will develop breast cancer before the age of 85 and approximately 13,000 new cases of breast cancer are diagnosed each year in Australia. The aim of the Mammary Gland Biology Group is to understand the cellular and molecular mechanisms that underpin breast cancer susceptibility, with the goal of developing new therapies to reduce the incidence and risk of breast cancer.

The aim of our research is to understand why this tissue has such high susceptibility to cancer, with the hypothesis that altered immune system function is an underlying cause. The body has a number of systems in place to help repair DNA mutations when they occur, thus protecting the body from cancer. Cells of the immune system are part of the body's defence against cancer, and can recognise and eliminate cells containing DNA mutations. However, our research shows that in the mammary gland, immune cells called macrophages are also critical for the normal function across the ovarian cycle.

Our current research utilises a variety of sophisticated transgenic mouse models to investigate how macrophage functions in the mammary gland are regulated and how these functions affect cancer risk in this tissue.

Research outcomes:

- Research has shown that macrophages participate in mammary gland development and regression over the course of the menstrual cycle. These functions are dependent on the hormones and may be the link between high cumulative number of menstrual cycles and increased breast cancer risk.

CASE STUDY

IVF BREAKTHROUGH TO HIT THE WORLD MARKET

(Top) Professor Sarah Robertson

Professor Sarah Robertson has achieved a major breakthrough in IVF technology that is expected to help millions of women around the world who have suffered previous miscarriages after IVF treatment.

Professor Robertson, who is an NHMRC Principal Research Fellow, partnered with a Danish company to develop a product which improves IVF embryo implantation rates for some women by up to 40%.

In the world's largest clinical trial on IVF media, Professor Robertson and Origio a/s – a European company specialising in assisted reproductive technologies (ART) – have shown for the first time that growth factor molecules are critical to ensuring optimal embryo development.

The resulting product, EmbryoGen, to be released in 2011, contains a signalling molecule called GM-CSF found naturally in the mother's tissues which protects the embryo from stress, making it stronger and more robust in the early implantation period.

The clinical trial, involving 1319 IVF patients exposed to either EmbryoGen or standard IVF embryo media, resulted in an average 20% improvement in embryo implantation rates at 12 weeks for all IVF women whose embryos developed in EmbryoGen. The effect is primarily due to benefits for women who had previously miscarried, who showed an impressive 40% increase in implantation success.

"This is a wonderful advance for couples undertaking IVF, particularly those who have previously lost babies in the first trimester," Sarah says.

It is also the culmination of more than two decades of work for Sarah, who based her PhD on the role of growth factors in healthy pregnancies and then worked with Swedish colleagues to explore applications in IVF embryos.

"This breakthrough has been 20 years in the making," Sarah says. "It's enormously rewarding to see one's basic research translate into practical outcomes that will benefit so many families."

"From day one we went right back to the fundamental biology to see what makes an embryo healthy in its normal environment in the reproductive tract. We discovered that the embryo is exposed to growth factor signals from the mother's tissues, which is critical to its optimal development.

"This is a major paradigm shift for reproductive medicine. All of the other ART companies around the world, along with biologists and clinicians in this area, have thought that embryos don't need growth factors.

"We have demonstrated through extensive animal and human clinical trials that the reality is just the opposite. EmbryoGen is not only completely safe and natural – it contains signalling molecules that the embryo expects to find in the mother's body – but our data from animal studies shows that it may also result in IVF babies that are larger and healthier at birth."

Sarah says IVF children are often smaller at birth, sometimes leading to long-term effects in later life.

"By adding back this growth factor and protecting the embryo from stress, the result should be babies that are of a similar size to those naturally conceived." The data on the perinatal outcomes will be available later this year.

EmbryoGen will be launched in Europe and the Middle East by mid 2011 and in the USA in late 2012.

Menopause and Reproductive Endocrinology

Research leader:
Professor Alastair MacLennan AO

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

Research outcomes:

- Completed contribution to a multicentre international clinical trial of a new contraceptive patch. The trial was funded by a research grant from Bayer HealthCare.
- Continued to contribute to local educational and research meetings of the Adelaide Women's Health Group.

Obesity and Insulin Resistance

Research leader:
Associate Professor Leonie Heilbronn

IVF currently accounts for 1 in 30 live births in Australia, and there are over 70,000 IVF individuals in Australia today, with over 10,000 IVF babies born each year. New evidence suggests that these individuals may be at higher risk of developing obesity, cardiovascular disease (CVD) and type 2 diabetes. The Obesity and Insulin Resistance Group aims to quantify the extent of their impairment of metabolic and cardiovascular health, including their sensitivity to challenge by an obesogenic diet.

Recent studies suggest that adult mice conceived in vitro have a hyperinsulinaemic response to an intraperitoneal glucose tolerance test, as compared to mice conceived in vivo, despite similar body weights, and have increased systolic and diastolic blood pressure at 21 weeks of age. Increasing reports suggest that the metabolic health of IVF-conceived children may also be altered. Since the use of IVF is increasing in the community, it is important to examine this in adulthood, and to quantify the future potential health costs.

Participants aged 18–25, born either following an IVF procedure or conceived naturally, are being recruited and fed a weight-maintenance low-fat diet for 3 days, followed by a high-fat overfeeding diet for 3 days. Participants are assessed on each occasion for insulin sensitivity by clamp, resting energy metabolism, blood pressure and lipids, and a muscle and fat biopsy is taken to measure DNA methylation changes. Body composition is assessed by dual X-ray absorptometry (DXA) scanning.

This study commenced in October 2010 and the group has studied 12 patients to date.

Oocyte Biology

Research leader: Dr Robert Gilchrist

The Oocyte Biology Group is interested in the molecular determinants of oocyte developmental potential. The research aims to improve the treatment of female infertility and ovarian dysfunction.

Our research investigates the molecular and cellular processes regulating oocyte-somatic cell communication and how these impact on the capacity of the oocyte to support optimal development of the embryo/fetus and ensuing offspring.

Research outcomes:

- Published the details of a novel oocyte in vitro maturation procedure (SPOM) that substantially improves embryo and fetal development.
- In partnership with Johan Smitz and others in Brussels, provided proof-of-principle of SPOM using human oocytes and established a multiparty collaboration to conduct a clinical trial.
- Translated basic discovery research to clinical practice. SPOM is entering a multicentre phase III clinical trial. The group has received NHMRC funding to also continue animal studies to further develop the procedure for future clinical applications.
- Provided insight into the molecular mechanism by which GDF9 and ERK1/2 signalling interact in ovarian granulosa cells.

Ovarian Cell Biology

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

The Ovarian Cell Biology Group is elucidating how the microenvironment within the ovary determines the quality of oocytes and the timing of their ovulation in order to generate new knowledge about how to better promote or to prevent female fertility. Understanding how the ovary nurtures oocytes to regulate their growth, maturation, ovulation and fertilisation is essential for optimising fertility.

Ovulation is a key biological process that has been clinically manipulated for decades to either promote or prevent the ability of women to conceive. However, the normal cellular mechanisms that control this process – which is fundamental to the reproductive health of women and the continuation of species – are not known.

Approximately 52% of Australian women are overweight or obese, which has serious health consequences on infertility. Obesity is a risk factor for anovulation including the increasingly common failure to respond to gonadotropin treatment in assisted reproductive therapy (ART). Furthermore, even in women who are experiencing regular cycles, obesity is associated with increased time-to-pregnancy and decreased chance of pregnancy. Most alarming, obesity appears to be a self-perpetuating cycle that is transmitted from mothers to the next generation by the periconception environment of the oocyte.

Our research spans many parallel projects that are determining the cellular mechanisms that regulate ovulation and how ovarian cells operate as the communication nexus between the maternal environment and embryo developmental potential. We use cutting-edge molecular and cell biology techniques to investigate the processes in ovarian cells that ensure production of high quality oocytes.

Research outcomes:

- Discovered and characterised the molecular and biochemical aspects of the lipid metabolism pathway in ovarian cells and embryos. This provides new mechanistic insight into how modern lifestyle perturbations such as fatty diet disadvantageously impact ovarian function and fertility. We produced the first demonstration that excess lipids induce endoplasmic reticulum stress in the ovary, decreasing oocyte health.
- Characterised new genes in human ovarian cells that determine the capacity of oocytes to form healthy pregnancy. This offers a simple, non-invasive biomarker to interrogate the oocyte's developmental potential in IVF. A provisional patent has been filed on this novel application that may revolutionise efficiency and quality of outcomes in fertility clinics and animal production.
- An important innovative aspect of our research offers to identify medical alternatives to IVF by revealing functions of ovarian cells and extracellular proteins that promote oocyte maturation. We have characterised essential genes that are induced in ovarian cells surrounding the oocyte and their role in oocyte maturation and ovulation. This information is being capitalised upon to develop therapies that avoid IVF for many infertile patients by restoring their ovarian function.
- Other recent work characterising the mechanism of hormonally controlled ovarian lymphatic system development has helped define the basis for aberrant responses to hormone treatment in ART patients.

Ovarian Follicular Development

Research leaders: Professor Ray Rodgers and Dr Helen Irving-Rodgers

The goal of the Ovarian Follicular Development Group is to discover key aspects of follicular development that underpin our understanding of infertility and endocrine diseases involving the ovary, and to develop prevention and treatment strategies for these.

A woman's health and wellbeing can be adversely affected by the ovary. Common conditions include polycystic ovary syndrome, affecting an estimated 5–7% of women, and premature ovarian failure, affecting about 1% of women under 40 years of age.

Recently we have made a big investment in developing screening technologies. We are gaining experience in how to maximise the utility of the data we collect by identifying which are the important molecules, pathways and processes to follow up on. We have also been consistently translating our observations and discoveries from the bovine model to the human ovaries.

Our basic studies are important to fill gaps in knowledge and to discover how the ovary functions normally and what potentially can go wrong. Ideally, these discoveries will be used to treat or prevent infertility or endocrine conditions involving the ovary.

Research outcomes:

- Investigated the roles of extracellular matrix molecules in the development of the ovary and published a comprehensive examination of a multitude of extracellular matrices in the ovaries of mice, an important laboratory experimental model. We also published a seminal paper on how to classify ovarian follicles.
- Developed a hypothesis on follicular fluid formation that production by the follicular cells of the extracellular matrix molecules hyaluronan and versican generates an osmotic gradient to draw in fluid from the surrounding cellular layers.
- Identified a novel type of basal lamina matrix, which we called focimatrix. It is developmentally regulated in the later phases of follicular growth. Our recent data suggest that focimatrix is the key to a follicle developing dominance over other follicles in the follicular phase of the cycle. It may achieve this by stimulating follicular cells to produce progesterone.

PCOS, Fertility and Reproduction

Research leader: Professor Robert Norman

The PCOS, Fertility and Reproduction Group seek to deliver better health outcomes for women with reproductive disorders, especially polycystic ovary syndrome (PCOS). We are also addressing the role of diet and nutrition in the aetiology and treatment of PCOS and other diseases.

We continue to investigate appropriate preconception approaches for women and men with infertility to optimise their chances of spontaneous pregnancy and a healthy start to life for their baby. We are also collaborating with Dr Robker and her group on the relationship between obese women (with and without PCOS) and oocyte biology.

Research outcomes:

- Groundbreaking systematic reviews on lifestyle, PCOS and metabolic disorders.
- First description of metabolic disorders in the follicular fluid of obese women undergoing IVF.
- Collaborated with the Jean Hailes Foundation for Women's Health to develop new guidelines for PCOS, funded by the Federal Government. This involved a systematic review of the literature, preparation of the evidence for interventions, and submission of formal guidelines to the NHMRC.

Placental Development

Research leaders: Professor Claire Roberts and Professor Gus Dekker

The Placental Development Group focuses on the cellular and molecular mechanisms by which the placenta develops and influences pregnancy success.

Recurrent miscarriage, preeclampsia, preterm birth, intrauterine growth restriction and gestational diabetes afflict around 1 in 4 pregnancies. Defects in how the placenta develops in early pregnancy can predispose the pregnancy to such complications. However, we do not know which women in first pregnancy are at risk until symptoms become evident. Therefore, we are developing tests to predict which couples are at risk of developing pregnancy complications long before symptoms arise.

The group's research encompasses both basic and clinical research. We use in vitro and animal models to determine the cellular and molecular mechanisms that regulate key processes in the development of the placenta and fetal growth, as well as maternal adaptation to pregnancy. In addition, we study the human placenta in normal and pathological pregnancies. Our clinical research focuses on pregnancy cohorts, the best known of which is the SCOPE cohort, recruited prospectively and strictly monitored for pregnancy outcomes. These provide the clinical, lifestyle and psychosocial data, as well as comprehensive biobanks, in which to identify risk factors for developing pregnancy complications.

Research outcomes:

- Using a candidate gene approach, we have identified a number of genetic variants in genes that regulate placental development and maternal adaptation to pregnancy. We developed prototype algorithms to predict couples at risk of preeclampsia, preterm birth and small for gestational age infants. We are currently refining these algorithms and seeking a commercial partner to develop them for use in the antenatal clinic.
- Showed that men with a body mass index (BMI) greater than 30 and a waist circumference of over 102 cm are more likely to father a baby who is small for gestational age. So dads count after all!
- Completed an NHMRC development grant project that demonstrated that our new patented media formulation for embryo culture improves embryo development, implantation rate and pregnancy rate late in gestation without any deleterious effects on the mother.

Reproductive Cancer

Research leaders: Dr Carmela Ricciardelli and Associate Professor Martin Oehler

The Reproductive Cancer Group focuses on the identification of early ovarian cancer markers and new therapeutic targets to improve the survival outcome for women with ovarian cancer.

Each year over 1,500 women are diagnosed with ovarian cancer and around 900 die from the disease in Australia. The poor prognosis results from late diagnosis and ineffective therapies for advanced disease. Due to lack of early detection, ovarian cancer is the most lethal malignancy in women.

During 2010 the group focused on three core research projects: proteomics of ovarian cancer implantation; an immunoproteomics approach to identifying early detection markers in ovarian cancer; and interactions with tumour microenvironment.

Research outcomes:

- Identified several proteins which are specifically modulated by the ovarian cancer–peritoneal cell interaction,

including extracellular matrix protein, TGFBIp; the phospholipid calcium-binding cytoskeletal protein annexin A2; and transketolase, a cytosolic, metabolic enzyme that catalyses key reactions in glucose metabolism. Our findings indicate that TGFBIp is part of a tumor–host signal pathway between ovarian cancer and peritoneal cells which promotes metastasis of ovarian cancer cells onto the peritoneal surfaces and is therefore a potential novel therapeutic target against ovarian cancer.

- Demonstrated increased annexin A2 levels in serious ovarian cancer tissues compared to benign ovarian disease. Furthermore, we have shown that annexin A2 inhibitors can significantly block three key processes essential for ovarian cancer metastasis: cancer cell motility, peritoneal cell adhesion, and invasion. These findings strongly suggest that annexin A2 is actively involved in the process of ovarian cancer metastasis.
- Showed high transketolase expression in 50% of ovarian cancer and those transketolase inhibitors significantly reduced ovarian cancer cell proliferation in vitro. Our results suggest that inhibiting the TKT pathway that is essential for glucose metabolism for nucleotide production could be an effective new target for anti-cancer therapy in ovarian cancer.
- Demonstrated for the first time that ovarian cancer cells can assemble a pericellular matrix utilising the ECM components HA and versican that promotes their motility and invasion in vitro. These findings indicate a role for versican and HA in ovarian cancer metastasis.

Reproductive Immunology

Research leader: Professor Sarah Robertson

The Reproductive Immunology Group is focused on defining how cells and molecules of the immune system participate in embryo implantation and successful pregnancy, and how their dysregulation contributes to female reproductive disorders. In particular, we wish to understand how male seminal fluid, infection and environmental factors (such as stress and alcohol) influence female reproductive tract immune function and competence to establish pregnancy.

We are investigating the immunological and inflammatory causes of endometriosis, infertility, preterm delivery, miscarriage and preeclampsia.

Our group uses human tissues and animal models to interrogate how immune cells and cytokines control reproductive physiology and pathophysiology. Our strategy is to explore new biological paradigms in mouse models and then to utilise this knowledge to investigate human reproductive function and disorders.

During 2010, Dr David Sharkey, went to the laboratory of Dr Alison Quayle at Louisiana State University, New Orleans, where he gained skills and built collaboration in research on the significance of female reproductive tract chlamydia infection in the periconceptual environment.

The group also hosted the international Congress for Reproductive Immunology in Palm Cove, Cairns, which brought together world leaders in reproductive immunology to share and discuss the latest advances in how the immune system influences reproductive processes and fertility.

Alison Care

Research outcomes:

- Published high impact papers reporting that (1) seminal fluid promotes attraction of suppressor cells known as “regulatory T cells” into the uterus prior to embryo implantation by induction of MIP3B and other chemokines; (2) GM-CSF is critical for controlling dendritic cell populations and their antigen-presenting function within the uterus; (3) uterine macrophages and their secreted factors including LIF have a key role in controlling endometrial epithelial cell expression of fucosylated structures that mediate embryo attachment at implantation; and (4) interleukin-6 is an essential factor in the sequence of inflammatory events leading to uterine activation and on-time parturition. Projects on the effects of repeated seminal fluid exposure for pregnancy tolerance, TLR pathways in preterm labour, cytokine regulation of embryo development, and the importance of microRNAs in regulating endometrial function in early pregnancy also made exciting progress.
- Dr Hull’s endometriosis projects were also fruitful, with publications showing that microRNAs are implicated in the patho-genesis of endometriosis and appear to interact with gene polymorphisms to influence disease susceptibility.

FUTURE

In 2011 the Research Centre for Reproductive Health will focus on maximising opportunities for researchers to access the best possible research infrastructure through working with the Institute to consolidate our equipment and technologies in new core facilities.

Under development is the STARR laboratory that will offer first-rate imaging technology and support nanoscale-sensing technology for world-leading embryology research and advanced culture systems.

The Centre will also continue the expansion of laboratories for several research groups located in the University of Adelaide Medical School, where space constraints have long been a limiting factor.

A major ongoing activity will be 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.

Ongoing, the Centre will continue to develop the technical skills and research capabilities of our members through supporting interstate or overseas laboratory visits and workshops, and encouraging travel to the most relevant research conferences to showcase their research.

CASE STUDY

FERTILITY PRESERVATION CLOSER TO REALITY FOR FEMALE CANCER SURVIVORS

Dr Kylie Dunning was named the 2010 Young Investigator Award winner for her work to help preserve the fertility of female cancer survivors.

Kylie, a postdoctoral researcher, examined the role of fat metabolism in the growth and development of ovarian tissue in the laboratory.

“Major advances in medical research have led to improved cancer therapies and increased survival rates in patients, but the use of life-saving chemotherapy and radiation therapy often leads to infertility,” Kylie said.

“In Australia, girls as young as 13 years old affected by cancer can have a portion of their ovaries cryopreserved for future use. What we’ve discovered may increase the chances of these women starting a family later in life.”

The latest technology for female fertility preservation involves growing ovarian tissue in a three-dimensional ball of gel in the lab, enabling eggs to grow and develop surrounded by their support cells, known collectively as the follicle.

This technology enables the growth of eggs in the laboratory that can then be fertilised and form embryos as in traditional IVF. In the future, these embryos could be returned to the womb to form a pregnancy and a healthy baby. By using this technology, it avoids having to put back the cryopreserved ovarian tissue, which may contain cancer cells.

Kylie said the use of 3-D follicle growth was extremely promising; however, the growth of eggs capable of forming a healthy embryo and a baby required further development.

“I’ve found that fats are a vital energy source for follicle and egg development. In fact, we’ve discovered that increasing the follicle and egg’s utilisation of fat during 3-D follicle growth significantly improves subsequent embryo development,” Kylie said.

The Young Investigator Award, now in its 11th year, rewards scientific excellence in South Australia’s young researchers and their ability to communicate and “sell” that science. As winner, Kylie received The Hon. Carolyn Pickles Award of $10,000.

In 2010, Kylie was also awarded the highly prestigious Trainee Research Award from the Society for the Study of Reproduction. This international award recognises the best papers presented at the Society’s Annual Meeting by a predoctoral or postdoctoral trainee.

Cancer patient Grace Madigan 15 and Dr Kylie Dunning (courtesy The Advertiser)

Professor Stan Gronthos
and Professor Andrew Zannettino

CENTRE FOR STEM CELL RESEARCH

CENTRE DIRECTORS' REPORT

The Centre for Stem Cell Research brings together researchers with a common focus in stem cells at the University of Adelaide, and its researchers and affiliate title holders at the Women's and Children's Hospital, the Institute of Medical and Veterinary Sciences, 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 $6 million in research funding annually.

Our members undertake internationally recognised and awarded research in embryonic, adult and cord blood stem cell research across a range of areas including developmental biology, immunology and regenerative medicine.

Many of our research programs are focused on developing novel cures using stem cells, including repairing the damage to the brain following stroke; bone cartilage and tissue repair in general; blood disorders such leukaemia and genetic disease; cystic fibrosis; and lysosomal storage disorders.

During 2010, the Centre continued to institute a number of initiatives based upon its strategic plan to encourage collaboration amongst 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.

The Centre awarded three internal collaborative grants, designed to foster collaboration between Centre researchers and other researchers working in the field of stem cells. This program provides seed funding of up to $75,000 over 18 months to generate preliminary data in order to enhance the competiveness of applications to funding agencies.

Directors:

Professor Stan Gronthos

Associate Professor Mark Nottle

RESEARCH GROUPS

Acute Leukaemia

Research leaders:
Professor Richard D'Andrea and Dr Ian Lewis

Current treatments for acute myeloid leukaemia (AML) are not specific, have severe side effects and are not always effective at treating the disease. The Acute Leukaemia Group aims to improve understanding of the control of blood production and disease pathogenesis required to design targeted therapies that eradicate the disease.

The number of deaths from blood cancers each year is second only to lung cancer. There are 850 new cases of AML diagnosed each year in Australia. Our major focus is understanding the mechanisms underlying normal blood cell growth and differentiation, and the changes associated with initiation and pathogenesis of blood diseases.

We are using novel systems to dissect signalling pathways that control cytokine-induced cell survival, proliferation, differentiation and self-renewal. In particular, we are utilising molecular approaches to identify genes and factors that contribute to the therapeutic response and relapsed disease in AML. Finally we are investigating new approaches to monitor disease and classify AML patients using novel markers and bioassays.

Research outcomes:

- A novel determinant of response in AML. We identified the stress-induced tumour suppressor gene GADD45A (growth arrest and DNA damage inducible 45) as a down-regulated gene in AML and showed that silencing of GADD45A contributes to the growth, survival and blocked differentiation typical of AML cells. Recently, we discovered that GADD45A is associated with promoter hyper-methylation and silencing in a significant proportion of patient AML samples. Analysis of clinical outcome data shows that hyper-methylation in the proximal promoter of GADD45A defines a subclass of AML (over 30% of patients) with a particularly poor outcome, despite intensive chemotherapy. Importantly, we showed that in normal karyotype AML (NK-AML) this is predictive of outcome, independent of other key prognostic mutations such as those in FLT3.
- Treatment of AML with MLL translocations. MLL is an epigenetic modulator located on 11q23 that, when fused to binding partners, has the unique ability to confer stem cell renewal properties to committed progenitors. This subtype has a particularly poor prognosis. A recent body of work suggests there are intrinsic differences between MLL-leukaemic stem cells and normal haematopoietic stem cells that can be therapeutically exploited.

Allan Scott Cystic Fibrosis Research Laboratory

Research leader: Dr David Parsons

Cystic fibrosis (CF) is the most common inherited disease affecting Western society, with 1 in every 2,500 children being affected.

No cure is available and the current treatments can only (briefly) slow the destruction of the lung. The lung infections in CF patients are extremely difficult to treat, even with the strongest antibiotics and most innovative therapies currently available.

The only current "alternative" to a slow death from CF lung disease is a lung transplant. However, with the reducing road toll, there are fewer and fewer lungs available, and survival after a transplant is usually between 5 and 10 years.

The goal of the cystic fibrosis group is to produce an effective treatment – and hopefully a cure – for CF lung disease. We are developing gene therapy methods that will deliver the corrected CF gene directly to the defective airway cells within a modified virus particle. We are also developing novel synchrotron X-ray imaging techniques to assist us in rapid detection of successful changes to the physiology of the lung after treatment.

Through substantial philanthropic and hospital support, a new state-of-the-art laboratory is being constructed in the Gilbert Building on the Women's and Children's Hospital campus to support our studies designed to bring the gene transfer methods to clinical trials.

Research outcomes:

- Showed that the airway gene-transfer technique works for test genes in the lungs of three different animal species (two published papers, with one in preparation). Dr Alice Stocker received her doctorate in 2010 for her work developing the successful gene transfer methods.
- Successfully evaluated a number of new techniques to measure changes in airway health using synchrotron X-rays. Studies have been conducted largely in Japan, but recently we have started to use the Australian Synchrotron.

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. In 2006 it was the leading cause of death in Australia, taking a life nearly every 10 minutes. It also reduced 1.4 million people's quality of life through directly related disability.

Two major types of heart failure exist. Ischaemic heart failure makes up about 60% of cases and is caused by narrowing of coronary arteries which deprive 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 is researching how different types of stem cells from bone marrow could be used to regenerate and repair 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.

Developmental Genetics

Research leader:
Associate Professor Paul Thomas

The Developmental Genetics Group aims to identify genes that cause common childhood diseases affecting brain and gonad development, and to understand how these genes function using mouse models. This research provides new insight into how different genetic changes cause disease, as well as important information and strategies for better diagnosis, management and therapy for these disorders.

Our research program focuses on understanding the genetic and developmental basis of intellectual disability, epilepsy and XX male sex reversal.

Several years ago, we showed for the first time that changes in the SOX3 gene cause intellectual disability in boys. Since then, we have been investigating the role of SOX3 in brain development and neural stem cells using mouse models. To do this, we have recently established Adelaide's only Mouse Transgenesis Facility at the University of Adelaide and have embarked on several collaborative projects with other local and interstate researchers who are interested in using this technology.

In 2010, we joined with nine other groups across Australia to investigate the causes of epilepsy and to develop new therapeutic approaches for this important condition. This major research initiative is funded by a prestigious Program Grant from the National Health and Medical Research Council worth over $15 million.

Research outcomes:

- As part of our long-term goal of understanding SOX3 function, we have recently discovered a novel role for this gene in gonad development. Intriguingly, we showed that activation of the SOX3 gene during early ovarian development causes activation of the testis differentiation pathway, resulting in XX male sex reversal. In addition, we showed that changes in the SOX3 gene in humans also caused XX male sex reversal. This is the first time that SOX3 has been shown to cause sex reversal in mice and humans and provides unique insight into the genetic basis of disorders of sexual development and the evolution of sex determination in mammals. We published these discoveries in a landmark paper in the Journal of Clinical Investigation in December 2010.
- Our 2010 publication on the genetic basis of XX male sex reversal was selected as a Faculty of 1000 publication, indicating that it is in the top 2% of biomedical research publications.
- In conjunction with collaborators, our new NHMRC Program Grant on Epilepsy was awarded an NHMRC Excellence Award for the highest-ranking Program Grant in the 2010 round.

Mesenchymal Stem Cells

Research leader: Professor Stan Gronthos

The Mesenchymal Stem Cell Group aims to determine the safety and efficacy of mesenchymal precursor populations to regenerate functional tissues such as ligament, cementum, dentin, bone, cartilage, cardiac muscle and brain tissue when implanted into animal models of disease and tissue damage.

Professor Stan Gronthos was co-discoverer of adult human mesenchymal precursor cells from different tissues and has spent the last two decades characterising the properties of these stem cells, including their potential as therapeutic agents for various regenerative medicine applications.

The group is identifying factors and molecular signalling pathways that mediate mesenchymal precursor cell self-renewal, niche maintenance, proliferation recruitment/migration and multi-differentiation.

Research outcomes:

- Proteomic characterisation of mesenchymal stem cell-like populations derived from ovine periodontal ligament, dental pulp and bone marrow: analysis of differentially expressed proteins.
- Identification of a common gene expression signature associated with immature clonal mesenchymal cell populations derived from bone marrow and dental tissues.
- Enrichment for STRO-1 expression enhances the cardiovascular paracrine activity of human bone marrow-derived mesenchymal cell populations.
- Reparative effects of allogeneic mesenchymal precursor cells delivered transendocardially in experimental non-ischaemic cardiomyopathy.
- Cervical motion preservation using mesenchymal progenitor cells and pentosan polysulfate, a novel chondrogenic agent: preliminary study in an ovine model.
- Application of autologous bone marrow-derived mesenchymal stem cells to an ovine model of growth plate cartilage injury.

Professor Stan Gronthos

- EphB/ephrin-B interactions mediate human MSC attachment, migration and osteochondral differentiation.

Myeloma Research

Research leader: Professor Andrew Zannettino

The Myeloma Research Group's efforts centre on identifying the molecular and cellular mechanisms responsible for myeloma disease progression.

Myeloma is an incurable haematological malignancy that affects 1 in 10,000 Australians. The malignant antibody-producing plasma cells cause massive destruction of the skeleton, leading to focal osteolytic lesions, pathological fracture, spinal cord compression, hypercalcaemia and renal failure.

Current projects are focused on (a) determining the role played by hypoxia in multiple myeloma (MM) disease progression; (b) identifying novel bone marrow microenvironmental factors which may contribute to MM disease progression; (c) identifying novel agents to inhibit osteoclast-mediated bone loss and/or stimulate osteoblast-mediated bone formation; (d) identifying novel signalling pathways with roles in mesenchymal stem cell differentiation, which may be manipulated to increase bone formation in MM patients; (e) examining the skeletal and metabolic effects of tyrosine kinase inhibitor compounds.

Professor Zannettino has also provided guidance on both myeloma and supportive treatment strategies and has co-authored guidelines for the safe use of bisphosphonates and Clinical Practice Guidelines.

Research outcomes:

- Long-term imatinib therapy promotes bone formation in chronic myeloid leukaemia (CML) patients.

CASE STUDY

HARNESSING STEM CELLS TO REPAIR BONE

Two leading researchers of the Centre for Stem Cell Research have been instrumental in developing a therapy that is likely to have a **significant impact in the treatment of spinal fusion, osteoarthritis, congestive heart failure, heart attacks, eye diseases, diabetes and bone repair**.

Professor Stan Gronthos and Professor Andrew Zannettino, based within SA Pathology, have conducted an innovative project which has led them to become co-inventors of a Mesenchymal Progenitor Cell (MPC) therapy that is now a step closer to the clinic after being commercialised by Mesoblast Ltd, a world leader in the development of regenerative medicine products.

The research has identified different mesenchymal stem cell (MSC) populations that live in adult bone marrow, peripheral fat and dental pulp tissue. These stem cells have the capacity to differentiate into connective tissue cell types and form the tissues from which they were initially derived.

The research formed the basis of the development of several patents encompassing the isolation and expansion technologies and use of different MSC preparations for various tissue engineering based applications.

“In mid 2010, the Australian Therapeutic Goods Administration issued a licence to our commercial partner, Mesoblast Ltd, approving the use of autologous MPC for the repair of skeletal tissues,” says Professor Zannettino.

Under this licence, Mesoblast will provide doctors and hospitals across Australia with the manufactured MPC products.

“Mesoblast will initially target major bone repair markets, including long bone fractures after trauma, stress fractures following sporting injury, and vertebral fractures due to osteoporosis,” says Professor Gronthos. “The cells will be manufactured under an agreement between Mesoblast and the TGA-licensed contractor Cell Therapies Pty Ltd.”

This research provides a significant leap forward in the treatment and regeneration of bone and joint conditions, an area that has traditionally been difficult to treat after significant damage or disease.

- Disruption of the CXCL12/CXCR4 axis inhibits osteolysis in a murine model of myeloma-associated bone loss.
- Hypoxia-inducible factor-2 is a novel regulator of aberrant CXCL12 expression in multiple myeloma plasma cells.
- NVP-BEZ235, a dual pan class I PI3 kinase and mTOR inhibitor, promotes osteogenic differentiation in human mesenchymal stromal cells and may be a novel treatment modality for myeloma-associated bone loss.
- Plasma adiponectin levels are markedly elevated in imatinib-treated CML patients: a mechanism for improved insulin sensitivity in type 2 diabetic CML patients.

Periodontal Stem Cell

Research leaders: Professor Mark Bartold and Professor Stan Gronthos

The Periodontal Stem Cell Group aims to utilise mesenchymal stem cells (MSC) and induced pluripotent stem cells (iPS) to repair and regenerate periodontal tissues affected by periodontitis. We are looking at new ways to grow new bone, cementum and periodontal ligament in periodontal defects.

The group is addressing this through utilising large (sheep) and small (rat and mouse) models of periodontal disease and implanting MSC and iPS into artificially created periodontal defects while also addressing fundamental cell biology of these cells through cell culture, molecular biology and immunohistochemistry.

Research outcomes:

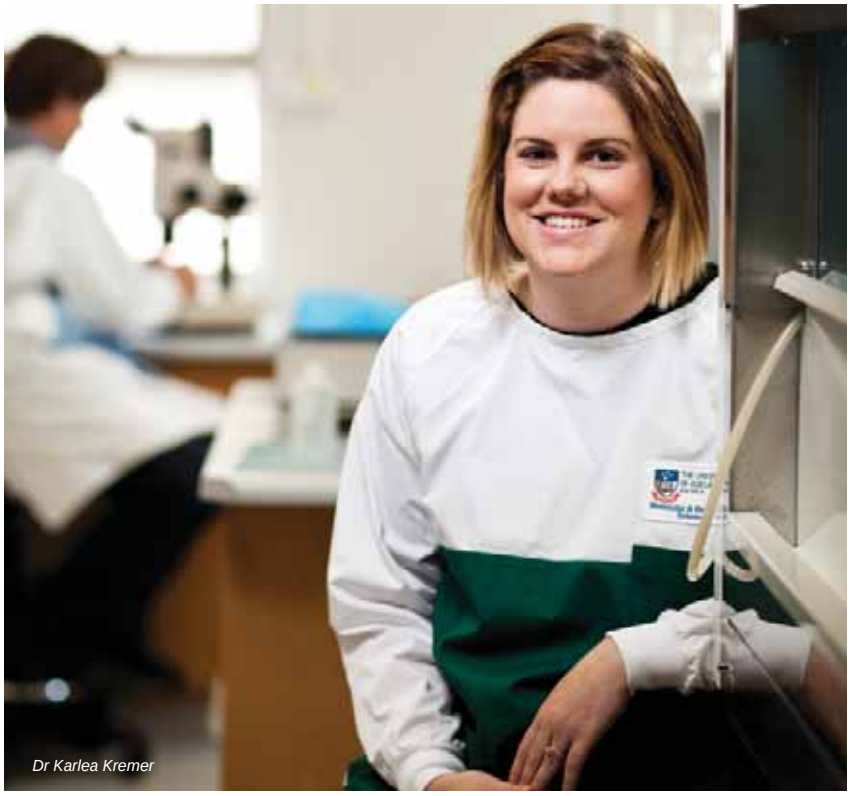
- Large (sheep) clinical studies have been completed and the retrieved tissues are now under analysis.
- Completed proteomic assessment of mesenchymal stem cells derived from periodontal ligament, bone and dental pulp.
- Successfully generated iPS cells from human gingival and periodontal ligament.

Reproductive Biotechnology

Research leader: Associate Professor Mark Nottle

The Reproductive Biotechnology Group is focused on isolating embryonic stem cells, as well as other stem cell types, from the pig for a variety of agricultural and biomedical applications. This includes the use of these cells to model the use of human stem cells for cell-based therapies.

We have developed a new method for isolating embryonic stem cells. Using this method we have isolated several embryonic stem cell lines from porcine embryos. These have been extensively characterised in vitro, including the production of various cell and tissue types such as neuronal and pancreatic islet precursors. In humans, the production of these (and other) cell types has the potential to cure a range of diseases including type 1 diabetes, as well as repairing the damage to the brain following a stroke. The use of these cell types from the pig will allow researchers to model these therapies in mouse and other animal models before using human embryonic stem cells in clinical trials.


Dr Karlea Kremer

Research outcomes:

- Development of a manuscript describing the isolation of embryonic stem cells from cloned embryos was accepted for publication in Cellular Reprogramming. The approach described in this paper allows embryonic stem cells to be isolated directly from any animal (male or female). The approach also provides a large animal model for so-called therapeutic cloning for the production of “personalised” embryonic stem cells which are not rejected by the body, thus overcoming the need for immunosuppression.

Stroke Research Program

Research leader:
Associate Professor Simon Koblar

The Stroke Research Program aims to understand how to repair the brain following ischaemic stroke, in order to assist the return of stroke patients to full function.

We seek to understand the role of Npas4, a transcription factor and regulator of GABAergic connectivity and neurogenesis, in the developing brain. We are also investigating the effect that implanted dental pulp stem cells (DPSC) have on repairing the brain after stroke, as well as other projects that help patient function.

In 2009–10, we undertook our first pre-clinical study using DPSC in a rat model of stroke. At 24 hours after stroke, we injected 600,000 adult human DPSC into the stroke brain. The animals were closely monitored for four weeks after treatment and we found a significant neuro-behavioural improvement following DPSC treatment in comparison to control animals.

Research outcomes:

- Completed a study of endothelial function and genetic polymorphisms in cerebral small vessel disease.
- Concluded a study of genetic polymorphisms and stroke in the gene PDE4D.
- Concluded the first pre-clinical study of DPSC therapy in a rat model of stroke, which is now being prepared as a manuscript for publication.
- In 2010, the Acute Stroke Unit, set up by members of the Stroke Research Program at The Queen Elizabeth Hospital and headed by Dr Jim Jannes, was funded for daytime operation seven days per week and, in preliminary figures, has resulted

in a halving of the number of deaths in patients presenting at the Unit compared to the previous corresponding period before the Stroke Unit was established.

Transplantation and Renal

Research leader: Dr Toby Coates

The Renal and Transplantation Group is developing cell-based therapies to repair and replace tissues and to prevent rejection of transplanted organs (dendritic cells).

About 10,000 Australians receive dialysis and over 1,000 are on the waiting list for a kidney transplant. The majority of those on the waiting list are aged less than 55 years and 83% are waiting for their first transplant.

We are using cell-based treatments as novel alternative therapies for organ regeneration and to improve the success of organ and tissue transplantation. We use dendritic cells as novel cells to modify the immune system in organ transplant recipients. These cells, which are derived from stem cells, can alter how the immune system sees foreign tissues and can potentially induce organ transplant tolerance.

We are also transplanting pancreatic islet cells to treat and cure type 1 diabetes as an alternative to insulin treatment. We are using mesenchymal stem cells, endothelial progenitor cells and dendritic cells to improve the outcome of transplanted organs or to repair damage of transplanted organs.

Research outcomes:

- In 2010, we have incorporated endothelial progenitor cells into chimeric islet clusters for the first time, an approach that has the potential to improve the blood supply and function of these delicate cells after transplantation.
- In the dendritic cell field, we have developed novel liposome-based approaches that can deliver drugs specifically to immune cells in the body. These approaches are being extended into non-human primate models, with the potential to modify the immune system to facilitate organ engraftment.
- We have also developed techniques and approaches to allow growth of large numbers of mesenchymal stem cells, which will be tested in kidney transplant models in 2011.

Vascular Biology and Cell Trafficking

Research leader: Dr Claudine Bonder

The Vascular Biology and Cell Trafficking Group has a focus on immune dysfunction and disease, through studying the intricate network of blood vessels which contribute to life-threatening diseases but are also essential for tissue regeneration and organ transplantation. The ultimate aim of this research is to provide new opportunities to augment blood vessel development in patients with cardiovascular disease and to reduce blood vessel development in cancer patients.

Cancer and cardiovascular disease are the major killers in the Western world. They place more social and financial burden on individuals, their families, society and government funds than all other diseases combined, with direct health care costs amounting to almost $10 billion per year. Current therapies tend to prolong life by a few months or years, but rarely cure the diseases. Our vision of examining blood vessels in disease is of national benefit as it will target cancer and cardiovascular disease and help us to come closer to long-lasting therapies and perhaps cures.

A major focus of the group is to identify new endothelial progenitor cell (EPC) biomarkers that define a purified population of cells with postnatal vasculogenic potential, as well as the genetic profile that regulates their differentiation, survival and recruitment. These observations open the door, for the first time, for the full characterisation of EPCs for diagnostic and therapeutic purposes for cardiovascular disease and cancer.

Research outcomes:

- Defining a new EPC signature. To overcome the problems that preclude the clinical investigation of EPCs, we recently developed a protocol for human and rodent EPC isolation, culture and expansion. We have also made key discoveries in EPC differentiation, where we observed that the enzyme sphingosine kinase-1 (SK-1) regulates the rate and direction of EPC differentiation without effect on the haematopoietic compartment.
- Recently executed the first gene expression analysis between naturally occurring human EPCs and their donor-matched mature blood vessel endothelial cells.
- Description of a new survival pathway by endothelial cells. We recently demonstrated that under basal conditions SK-1, integrin avb3 and CD31 (platelet endothelial cell adhesion molecule, PECAM-1) exist as a heterotrimeric complex and that in conditions which impact on EPC survival, increased formation of this complex occurs.

FUTURE

The Centre for Stem Cell Research, together with the Robinson Institute, is looking to attract a Robinson Postdoctoral Fellow in the area of induced pluripotent stem cells in 2011. This and future fellowships will be part of a new collaborative grant scheme designed to develop new research areas to enhance the Centre's research profile.

The Centre and the Robinson Institute are also aiming to attract funding for various research initiatives through the recently formed Robinson Institute Foundation and the Peter Couche Foundation (which specifically supports stem cell for stroke research).

(Right) Associate Professor Simon Koblar and Peter Couche

Dr Natasha Rogers

CASE STUDY

SPICE OF LIFE FOR TRANSPLANT PATIENTS

In 2010, PhD student Dr Natasha Rogers was awarded three prestigious awards for her work to improve organ transplant success rates.

Natasha won the Ross Wishart Memorial Award for the best young medical researcher in South Australia and the President's Prize for the Best Research Presentation at the annual meeting of the Transplantation Society of Australia and New Zealand, as well as being the national winner of the AusBiotech-GSK Student Excellence Award.

The transplantation immunology researcher and her Queen Elizabeth Hospital colleagues are trialing an extract from the spice turmeric to counter damage caused by organ rejection. The turmeric extract, called curcumin, has both antioxidant and anti-inflammatory properties which limit the damage caused by an interruption to blood flow.

"The current problem with transplants is that when an organ, such as the kidney, is taken from an organ donor, the blood flow is stopped," Natasha said. "Once transplanted into a patient, blood starts flowing through it again and this blood flow can cause further damage."

This is called ischaemia-reperfusion injury, where the sudden return of blood flow, and the immune cells and oxygen that come with it, actually damage the newly transplanted organ.

"This is a significant problem in transplantation and affects the function of a transplant so that people might have more complications, such as rejection," Natasha said.

However, curcumin is not well absorbed by the body when swallowed and Natasha is establishing a new technique to deliver curcumin throughout the body, using microscopic fat particles called liposomes.

They found that curcumin contained within liposomes was taken up by immune cells in the body, successfully limiting the damage caused by an interruption to blood flow.

"We certainly hope that it could be used in humans in the future, but not just for transplantation. Curcumin could potentially be applied to treat other causes of ischaemia-reperfusion injury, such as heart attacks and strokes," Dr Rogers said. "Curcumin in this form is a safe treatment with no known side effects."

The next step will be trialling the curcumin liposomes in a mouse model of transplantation to see if it can reduce transplant organ rejection and improve transplant survival.

Dr Natasha Rogers completed her PhD in transplantation immunology under the supervision of Dr Toby Coates.

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Wai Sun

Professional Staff

Alissa Nightingale
Imogen Craig
Jackson Jaensch
Joanna Close
Karen Hannah
Leanne Srpek
Virginia Furness

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For further information:

The Robinson Institute
The University of Adelaide
Ground Floor, 55 King William Road
North Adelaide SA 5005

T: +61 8 8303 8166
F: + 61 8 8313 1355
E: robinsoninstitute@adelaide.edu.au
W: www.RobinsonInstitute.edu.au

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