



THE UNIVERSITY
of ADELAIDE



Annual Report 2013

Robinson Research Institute

seek LIGHT

Robinson
Research Institute
Healthy children for life.

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Vision

Our vision is to achieve life-time health for all children and families, through research excellence.

Mission

Our mission is to deliver world-leading advances in knowledge of human reproduction, pregnancy and child health, and to inform clinical care, policy and practice that will improve health across generations and global communities.



Message from the Deputy Vice-Chancellor Research

Outstanding research universities provide society with the fruits of their endeavours and bring about improvements in people's lives.



At the University of Adelaide we have established five research institutes which have been tasked with addressing 'grand challenges' affecting our communities now and into the

future. One of these challenges is securing a healthier future for our children. This is closely aligned with one of the highest level objectives of the South Australian State Government in "giving our children every chance to achieve their potential in life".

The Robinson Research Institute aims to uncover the factors that influence health across our lifetime and across the generations. With over 400 talented scientists and clinicians, the Institute is advancing knowledge and making significant improvements in fertility, pregnancy and child health.

In 2013, the researchers identified a promising biomarker and therapeutic target for ovarian cancer; changed understanding of how progesterone is produced to initiate pregnancy; demonstrated that diet during pregnancy influences the risk of preterm delivery; and the Institute's vaccine research was included in the NHMRC's Ten of the Best Research Projects 2013 – a great accomplishment.

As you read through the stories within this report, you will appreciate the great breadth and depth of the research being undertaken at the Robinson Research Institute.

It has been a year of transformation and change for the Institute. We farewell Professor Robert Norman (AO), the founding Director, and also Mr Mark Coleman, the inaugural Chair of the Advisory Board. They were a formidable leadership team and I sincerely thank them for their outstanding efforts, dedication and contribution to building and shaping the Institute. We were delighted to welcome Professor Sarah Robertson as the incoming Director, and look forward to watching the Institute continue to thrive and

flourish under her vision and leadership.

I would personally like to commend members of the Institute for the enormous amount of work they have invested throughout 2013 in reshaping the organisation. This has delivered a clear vision and an organisational structure which will enable even greater collaboration among its members.

With this exciting future plan, excellent track record and growth in global reputation, the University's commitment to the Institute continues to strengthen and in August 2013 the Institute commenced its second 5-year term.

I am confident that the Robinson Research Institute will continue to bring to light new discoveries, and make major contributions toward the transformation of clinical care and policy for the health of all children and families.

Professor Mike Brooks

Deputy Vice-Chancellor and
Vice-President Research



Chair's report - 2013

2013 saw the Robinson Institute (renamed the Robinson Research Institute in 2014) continue to evolve, transform and adjust as it moves toward the adoption of a new model of across-Institute collaboration, vision and investment.

The *Reshaping the Robinson* cultural and operational change program is successfully transforming the Institute, shifting its structure from a collection of independently operating Research Centres, to integrated Themes and Research Priorities that focus on the major health burdens in fertility, pregnancy and child health. The Institute constantly strives to review and adapt to the dynamic environment in which it operates. While the embedding of the new model is an ongoing process, the Institute continues to lead the way and build on past strengths.

Significant achievements have been realised in further developing relationships with key external organisations, and in improving the alignment of operations between the Institute and the University's School of Paediatrics and Reproductive Health.

There has been an increased focus on the support of researchers and the effective delivery of research outcomes. These include a significant commitment to building a suite of Core Facilities. Access to these facilities will help to position the Institute more competitively for research funding and will support improved research outcomes.

The Institute also saw key changes in its leadership during the year 2013.

Change of Director

The Institute farewellled Professor Robert Norman (AO), founding Director of the Robinson Research Institute. We pay tribute to Rob's tireless leadership, wisdom and passion. Under his leadership the Institute grew from strength to strength into a world-renowned Institute poised for ongoing success. During 2013, Rob was recognised with two significant awards:

- > Office of the Order of Australia (AO) for his service to reproductive health
- > Distinguished Researcher Award of the American Society for Reproductive Medicine (ASRM)

Rob stepped down from the Director role in September 2013 but remains an active contributor within the University of Adelaide and to the Institute's research programs.

Following an international search the University was delighted to appoint Professor Sarah Robertson as the new Director of the Robinson Research Institute, commencing on 1 October 2013. Sarah is an international leader in reproductive science, and is very enthusiastic about her role and the Institute's potential to address the major health burdens associated with reproduction, pregnancy and child health.

Change of Chair

The Institute also farewellled Mr Mark Coleman, Chair of the Institute's Advisory Board. Mark was the inaugural Chair commencing in 2009; he stepped down from this role and the Board in July 2013. During his term, Mark was a trusted confidant and provided wise counsel and guidance that delivered strength to the board, the governance structure, management and the operations of the Institute. We have benefited enormously from his input and commitment and thank him for his professionalism and service.

Professor Mike Brooks, Deputy Vice Chancellor (Research), and an existing member of the Advisory Board, stepped into the role as 'Acting' Chair in the latter half of 2013 to support the new Director, and to facilitate the search for a new Board Chair. We are delighted that Professor Jock Findlay takes over as Chair of the Advisory Board from January 2014.

During the year the Board also farewellled members Gail Mondy and Marie Dziadek. We thank both of them for their contributions to the work of the Board, and the Institute generally.

The ongoing Board members – Justin Beilby, Jock Findlay, and Paul Rolan – have been with the Board from the outset. To each of them we acknowledge their commitment, considered guidance and general 'value-add', and thank them for this.

The Institute constantly strives to review and adapt to the dynamic environment in which it operates...

The Members of the Robinson Research Institute have again made many great strides in their research work and we take this opportunity to recognise and acknowledge their commitment, hard work and achievements throughout the year. We also thank the many members who have committed time and effort to the *Reshaping the Robinson* project.

On behalf of the Board, we acknowledge the ongoing support of the University of Adelaide. The strong commitment and associated investment from the University provides a firm foundation upon which the Institute can build.

Our thanks also go to Kate Irving, General Manager, and her team for great work during the year.

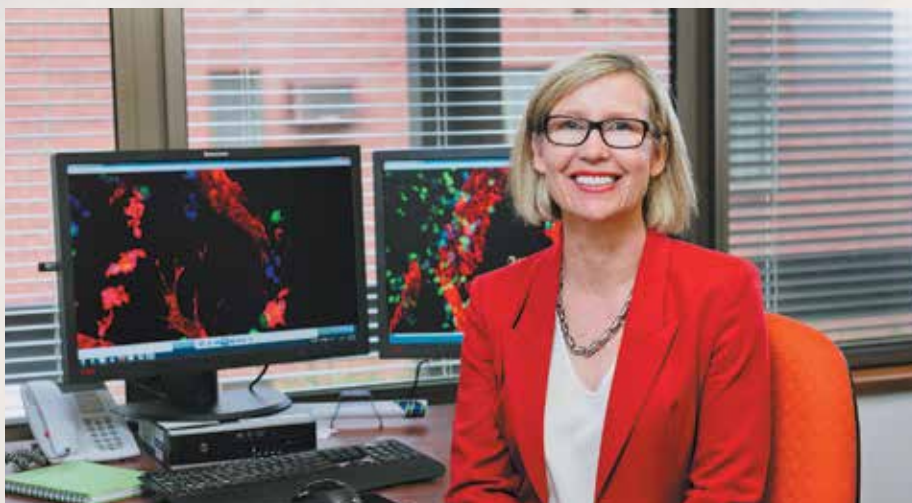
It has been an exciting year and we are confident in the Institute's continued success as it embarks upon the next chapter.

Mark Coleman, Chair
January – July 2013

Mike Brooks, Chair
July – December 2013

Director's report - 2013

As incoming Director from October 2013, I am excited to take on the challenge of leading the Robinson Research Institute into the future. In getting to know the 50 Research Leaders and their teams who make up our organisation, I am struck by the span of our research and the depth of our capability.



Within our ranks we have some of the most skilled and dedicated researchers in the country, with a remarkable richness of diverse and complementary skills and strengths. I am looking forward to supporting and enabling their important work.

The core motivation we share is to discover, to understand, and to direct the benefit of new knowledge to improving the health and quality of life of children and families in Australia, and across the globe. Our challenge, through the vehicle of the Institute, is to tackle the important and difficult research questions that are beyond our reach as individual researchers, but within our grasp if we pull together.

It is increasingly evident that to be relevant, to attract investment and to deliver value to our funding agencies and communities, we must focus on the critical knowledge gaps and collaborate in multi-disciplinary teams. Working together we can find solutions to assist healthy conception and pregnancy for intending parents, to reduce the horrendous rate of preterm birth that curtails the life

chances of 10% of children, to understand and alleviate the pregnancy disorders and early life events that contribute to childhood diseases such as obesity, diabetes, allergy and neurological impairment, and to develop new interventions that protect children from infection, disability and mental illness.

The major achievement of 2013 was to complete the task of reshaping the Institute. We deconstructed our component research centres, and built four new Themes that articulate the full scope of our research effort - Fertility and Conception, Pregnancy and Birth, Early Origins of Health, and Child and Adolescent Health. After extensive discussion and debate, we agreed on a series of Research Priorities, which describe the grand challenges we have set for ourselves. Already there is evidence of the benefits of bringing researchers together in new collaborations to address big questions in creative and constructive ways.

A second major initiative commenced in 2013 was the investment in core facilities. We made good headway towards building

capability in gene manipulation through the GSEx Facility, in supporting large-scale data analysis in the Bioinformatics Facility, and in delivering coordinated large epidemiological and mechanistic analyses through the Cohort and Intergenerational Studies Facility. These core services add to the existing Research Assay Facility to underpin the Research effort across all of the Themes and Priorities, and will become integral to many teams as services expand.

There are exciting times ahead as we establish a presence in the new West End precinct, engage with established networks locally and overseas, and build international partnerships with new collaborators and friends. There will be challenges to face as we come to terms with a difficult economic climate, and a contracting medical research funding base. Having repositioned our focus and embracing a team-based approach to address issues that have global significance, we are well-positioned to meet these head-on.

Although still relatively new in name, the Institute has origins founded 30 years ago reflecting Adelaide's traditional strengths in reproductive science and medicine. It is important to acknowledge the outstanding contribution of Professor Robert Norman, who stepped down as Inaugural Director in October 2013 after 5 years of extraordinary leadership. I also recognise the important contribution of our retiring Board Chairman, Mr Mark Coleman, and thank him for his service to the Board over the last 5 years.

Please read and enjoy this report, which celebrates many of the important discoveries made by our researchers over the last 12 months. These pages bring to life our contributions to expanding the horizons of human knowledge, and show the many ways we translate our discoveries to improve health, and to make a real difference in the world.

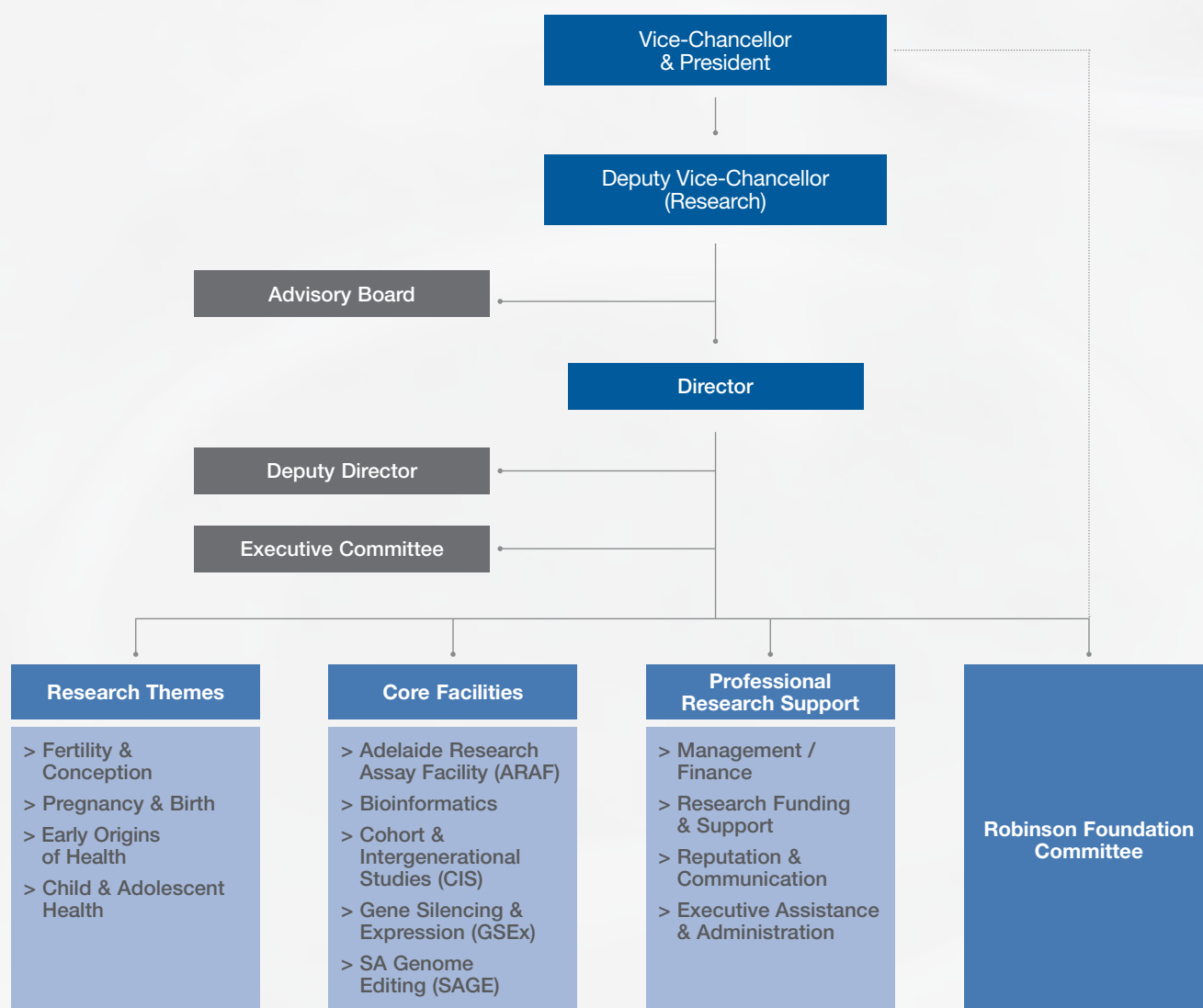
About the Robinson Research Institute

The Robinson Research Institute is a collective of internationally renowned researchers in human reproduction, pregnancy and child health at the University of Adelaide.

We focus on the early stages of life to improve the health and well-being of children and families over the life course and across generations, in Australia and around the world.

We seek to enable a healthy start through fertility choices and mindful conception, nurturing the baby during pregnancy and birth, strengthening the brain and body in early life, and advancing child and adolescent health to treat and prevent disease.

The Robinson Research Institute Structure



Robinson Research Institute at a glance



\$19.5m⁺
funding in 2013

50⁺
Research Leaders

\$140,000⁺
raised for the Peter
Couche Foundation

400⁺
Members

\$35,000⁺
raised for the Robinson
Research Foundation

4
Research Themes

10
Research Priorities



30⁺

Honours students

130⁺

PhD students

400⁺

publications

5

SA hospitals
embedded in

Affiliations

the School of Paediatrics
and Reproductive Health

Collaborations

Multiple national and
international

Future direction

Through 2013, the Robinson Research Institute continued to transition and embed the new operating model for future sustainability that stemmed from the Reshaping the Robinson project.



At the heart of this transformational change is facilitating greater internal collaboration. This is essential to allow our Institute to respond to the changing environment and funding challenges facing the research community globally.

Throughout the year the Institute and its members invested time and energy, to transition from a centre-based operating model to a theme-based research model, identifying and progressing Research Priorities, and developing a new vision and mission.

Widespread consultation, several workshops and open forum consultations have resulted in establishing four Research Themes that span the life cycle of human reproduction and health across generations.

Research Themes

Research Themes provide the necessary infrastructure and focus to operate as a Research Theme based organisation - enabling greater flexibility and cross collaboration. Our four Research Themes are:

Fertility and Conception
Pregnancy and Birth
Early Origins of Health
Child and Adolescent Health

The Research Themes cover the breadth of the Institute's research and align with the sequence of the reproductive process, articulating how our research improves health and wellbeing across generations. These Themes are inclusive of the fundamental issues affecting reproduction, pregnancy and child health, and have relevance to local, national and global communities.

Research Priorities

The development of Themes highlighted the need to identify Research Priorities. These require diverse expertise and cross-disciplinary, collaborative approaches to address issues of significant health burden nationally and internationally. They will enable the Robinson Research Institute to demonstrate distinction and achieve excellence in research outcomes.

By defining the Research Priorities upon which to focus and invest, the Institute will clearly demonstrate how its research is aligned to national and international priorities and how it can make a lasting impact. They will enable researchers from diverse fields and groups to come together, encouraging new ideas and perspectives to tackle some of the biggest research challenges that impact children and families worldwide.

The result of the research priority development process is the Institute's top ten Research Priorities:

Preventing and Alleviating Infertility: Enabling the best start in life
Fetal Growth: Understanding and optimising growth of the baby
Born Too Soon: Preventing preterm birth and improving outcomes for babies born preterm
Brain Power: Maximising neurodevelopmental potential
Parental Influences and Childhood Obesity: Preventing and reversing weight disorders
Reproductive and Childhood Cancers: Discovering causes and finding cures
Allergy: Researching origins of immune disorders
Mental Health: Improving the mental health of young people and their families
Protecting Children from Life-Threatening Diseases: Optimising prevention against serious infection
Treatment Innovations: Pioneering interventions to improve the health of children

Core facilities

As part of the Theme and Research Priority development process, the Scientific Review Panel was asked to make recommendations around how best to invest in our Research Priorities for the next three years.

During the process it was clear to the Panel that each Research Priority needed improved facilities, particularly in bioinformatics, gene manipulation, biostatistics and the management of cohorts and biobanks. Consequently it was recommended that the Institute invest in such facilities to deliver the greatest value.

In response to this recommendation the Robinson Research Institute has commenced the establishment of its Core Facilities. These are facilities that all researchers need and which the Institute is committed to building, they include:

Adelaide Research Assay (ARAF)
Bioinformatics
Cohort & Intergenerational Studies (CIS)
Gene Silencing & Expression (GSEx)
SA Genome Editing (SAGE)

2014 and beyond

2014 will be an exciting year for the Robinson Research Institute. The Research Theme based operating model will be in advanced stages of implementation, requiring the commitment and support of all research leaders, members and staff. This will be a great opportunity to create breadth and depth by exploring collaborative opportunities.

With a clearly defined vision, mission and Research Priorities, there will also be a renewed focus on raising funds. Working collaboratively with the University, the work of the Institute will be shared with the broader community to demonstrate the importance of ongoing funding for current and future generations.

As a leading research organisation in the field of reproductive, pregnancy and child health, the Robinson Research Institute will work closely with the South Australian Health and Medical Research Institute (SAHMRI) to develop our working relationship. The aim will be to leverage strengths and facilities, so both parties can contribute fully to the development of research in the state.

For 2014 and beyond the Institute will continue to foster an environment that encourages excellence in discovery and translation. By increasing collaborations and working with internationally renowned research leaders, we will ensure the highest standard of research is maintained and we open the doors to new possibilities in both applied science and basic research.

Since its beginnings, more than six years ago, the Robinson Research Institute has thrived under a leadership and culture of excellence, passion and innovation. Professor Sarah Robertson assumed the role of Director, succeeding Professor Robert Norman in October 2013. Sarah has a solid foundation on which to build - and her enthusiasm and focus on delivering excellence in research outcomes is a guiding principle that will see the Institute's reputation grow from strength to strength locally, nationally and internationally.

Advisory Board members



Mark Coleman
Chair Jan-July 2013



Prof Mike Brooks
Chair July-Dec 2013



Prof Justin Beilby



Prof Marie Dziadek



Prof Jock
Findlay AO



Gail Mondy



Prof Rob
Norman AO



Prof Julie Owens



Prof Sarah
Robertson



Prof Paul Rolan

Committee members

Transition Management Committee (Jan – Sep 2013)



A/Prof Vicki Clifton



Prof Jenny Couper



Prof Jodie Dodd



Kate Irving



Prof Rob Norman
AO Chair



Prof Julie Owens



Prof Sarah
Robertson



Prof Ray Rodgers



Prof Andrew
Zannettino

Executive Committee (Oct – Dec 2013)



A/Prof Simon Barry



Prof Jenny Couper



Prof Jodie Dodd



Kate Irving



Prof Julie Owens



Prof Claire Roberts



Prof Sarah
Robertson Chair



Prof Ray Rodgers



A/Prof Darryl
Russell



A/Prof Michael
Stark

2013 research highlights

Excellence in Research for Australia (ERA)

Excellence in Research for Australia (ERA) is an initiative of the Federal Government. ERA is a research quality and evaluation system developed by the Australian Research Council (ARC) in conjunction with the Department of Innovation, Industry, Science and Research.

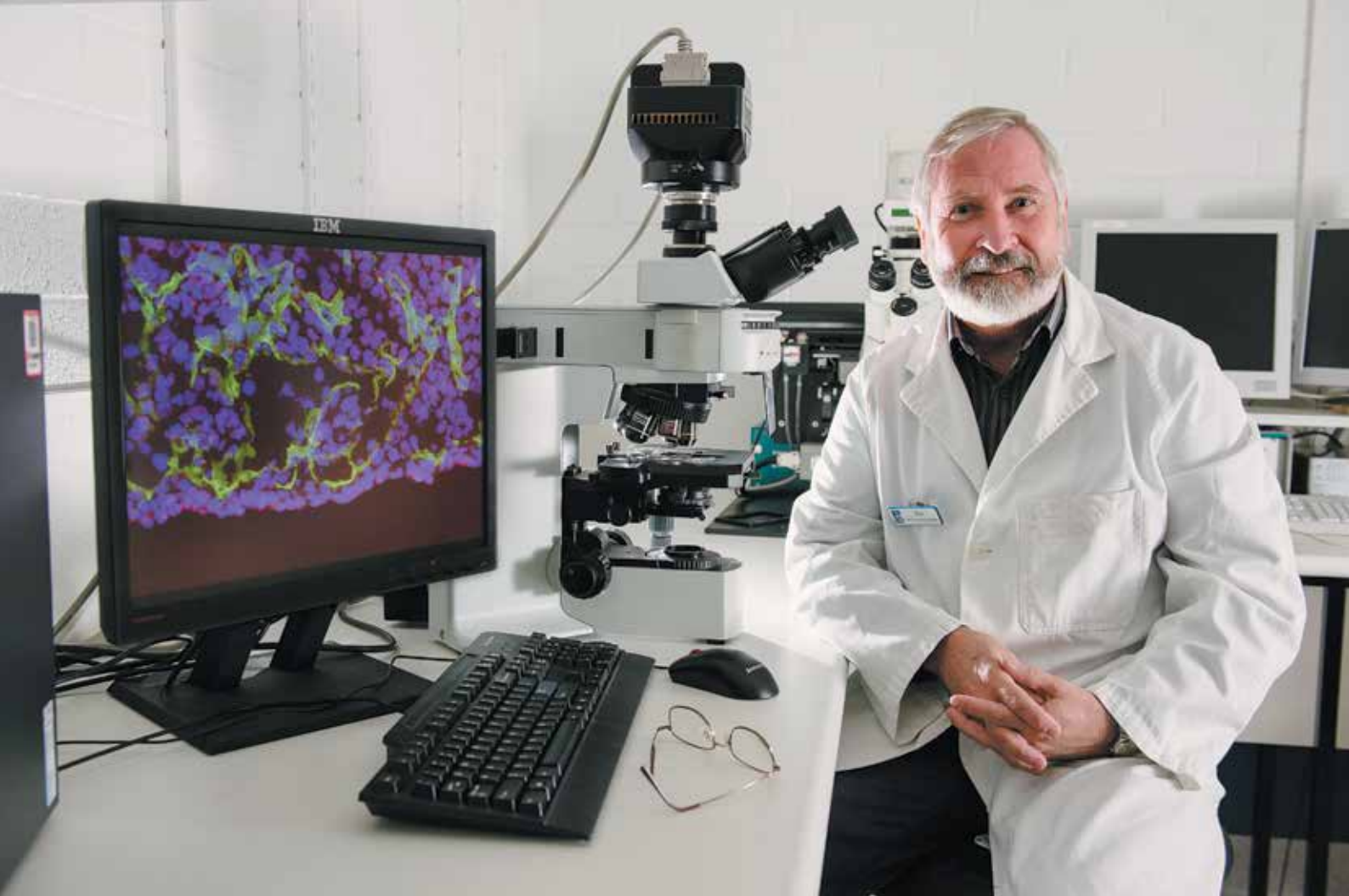
The ERA initiative aims to provide a transparent system to assess research quality, utilising a combination of metrics focused on publications and other research outputs, research income, esteem and applied measures. The information is reviewed at the national level by evaluation committees comprising experienced, internationally-recognised experts.

ERA results were released in 2010 and 2012. The Robinson Research Institute, through the School of Paediatrics and Reproductive Health, performed in the highest level in both rounds, ranking 5 – well above world standard. This cements the University of Adelaide's leading position in paediatrics and reproductive medicine – we are the only University in Australia to achieve this discipline ranking for the second time running.



Discovery highlights

- > **Helen Marshall and Michael Gold's research was included in the NHMRC's Ten of the Best Research Projects 2013.** Their research identified the serious complications associated with H1N1 influenza infection in children, and builds the case for promoting vaccination for the flu virus.
- > **Identification of the protein annexin A2 as a promising biomarker and therapeutic target for ovarian cancer.** Martin Oehler and Carmela Ricciardelli have shown that an annexin A2 neutralising antibody is effective at blocking ovarian cancer growth and spread in a mouse model.
- > **A newly discovered biomarker PI16 identifies immune-suppressive Treg cells which have a stable functional phenotype in healthy individuals.** Simon Barry, John Walsh and colleagues believe PI16 holds promise for detecting Treg cells exhibiting a loss of functional fitness in type 1-diabetes.
- > **Pro-angiogenic macrophages have an essential role in supporting embryo implantation and establishment of pregnancy.** Alison Care and Sarah Robertson demonstrated that pro-angiogenic macrophages stimulate development of the corpus luteum allowing sufficient progesterone production.
- > **Diet during pregnancy influences pregnancy outcomes.** Jessica Greiger and Vicki Clifton showed that women who consume a high fat and a high sugar diet are at increased risk of preterm delivery.
- > **Advances in our understanding of the importance of mRNA decay pathway (NMD) in neuronal cell behaviour.** Jozef Gecz and Lachlan Jolly have shown that NMD is an important therapeutic target for more than 2,000 genetic disorders by modulating the outcome of clinical presentations of genetic mutations.



- > **A model for delivery of Islet transplantation in Australia was created.** Toby Coates and colleagues showed that Islets isolated at a remote centre (Melbourne or Sydney) could be transplanted in Adelaide with excellent clinical outcomes.
- > **Identification of specific maternal and paternal genome effects on fetal muscle and bone development.** This includes implications of long non-coding RNA H19 in regulation of fetal phenotype. Stefan Hiendleder and colleagues' research provides the basis for molecular dissection of parent of origin effects to better understand fetal programming and postnatal phenotype.
- > **Endometriosis is associated with bone-like calcification.** Jonathan McGuane and Louise Hull found a link between proteins increased in endometriosis and bone regulatory factors, which seem to promote formation of calcified deposits in lesions.
- > **Allergy development may be programmed in utero.** Astrud Tuck and Vicki Clifton identified a number of genes that change expression in the placenta, and are associated with the subsequent development of an allergy in children.
- > **Identification of a new regulator of ovarian androgen production.** In a multicenter study, Ray Rodgers and colleagues showed that the hormone INSL3 regulates the CYP17 gene that encodes an enzyme needed to synthesise androgens.
- > **Discovery that the type and form of oocyte-secreted factors (specifically BMP15 and GDF9) added to IVM media is important for subsequent embryo development.** Jeremy Thompson and colleagues are focusing on optimising IVM to progress this technique to clinical use.
- > **Advances in our understanding of the protein TGFB and the role it plays in breast tumours.** Sally Sun and Wendy Ingman showed that TGFB not only affects the cells that form tumours, but also the surrounding macrophages and in turn the risk of tumour formation.
- > **Discovery of novel genetic variations that are likely to be causative both in families with members affected by cerebral palsy and in sporadic cases.** Alastair MacLennan and the Cerebral Palsy Research Group have shown that such variants align with the heterogeneity of the cerebral palsy phenotypes.
- > **Demonstrated the ability to induce late-phase neuroplasticity in the human cortex with multiple applications of a non-invasive brain stimulation (NIBS) protocol.** Michael Ridding's discovery has major implications for studying neuroplasticity and therapeutic applications of NIBS.
- > **Demonstration of the role of seminal fluid in regulating microRNA expression within the endometrial tissue of the female reproductive tract.** John Schjenken and Sarah Robertson's research provides new insights on immune adaptation immune adaptation at the outset of pregnancy.
- > **Demonstrated that novel small molecule inhibitors of Toll-like receptors are efficacious in preventing preterm birth induced by inflammatory challenge during late gestation in mice.** Sarah Robertson and Mark Hutchinson's research may lead to new strategies to prevent preterm birth.
- > **Discovery of a new model for how the ovary develops.** Ray Rodgers and colleagues have mapped cell fate decisions in fetal ovaries to identify and isolate novel GREL (gonadal ridge epithelial-like) cells from fetal ovaries.

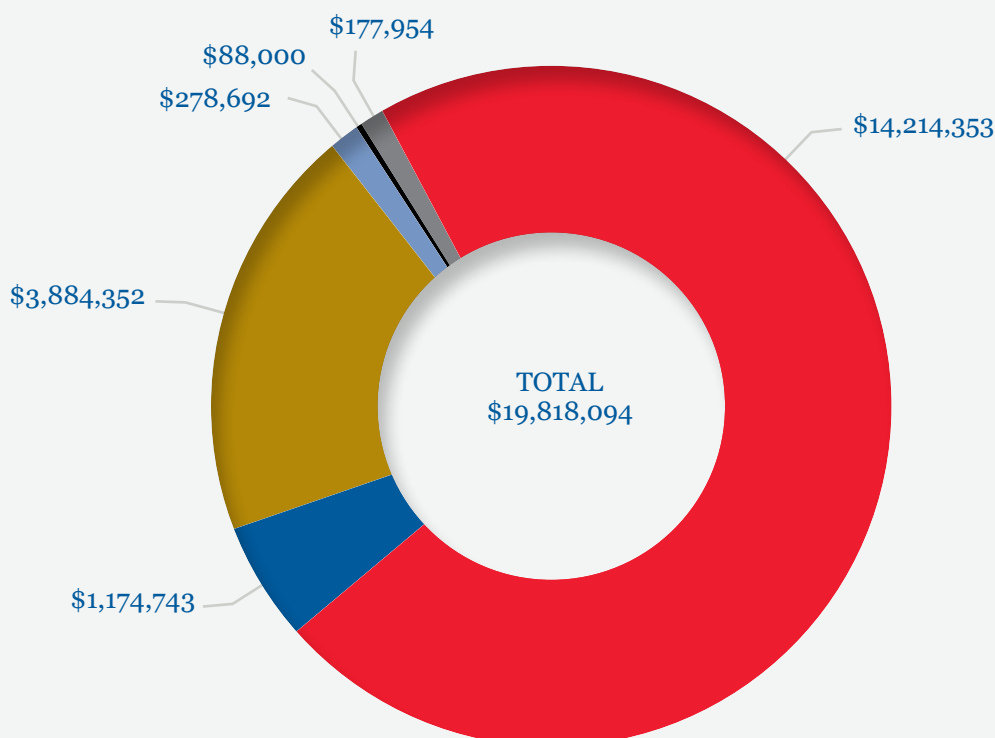
- > **Development of a novel diagnostic tool to predict early neonatal brain injury in extremely preterm newborns.** Michael Stark and Chad Anderson based this tool on prevailing cerebral oxygen kinetics.
- > **Oxford University Press published Dominic Wilkinson's book *Death or Disability? The 'Carmentis Machine' and decision-making for critically ill children*.** This book looks at the profound and contentious ethical issues facing those who work in intensive care caring for critically ill children and infants.
- > **Generation of knockout (KO) mice using genome-editing technology.** Paul Thomas and colleagues have implemented new tools to generate KO mice within weeks instead of months. This has huge implications for biomedical research.
- > **Demonstrated that the widely used IVM additives (FSH and EGF) are inadequate propagators of the essential EGF-like peptide signaling cascade.** Jeremy Thompson showed the use of epiregulin and/or amphiregulin during IVM leads to improved oocyte developmental competence and may be preferable to existing treatment protocols.
- > **Documented that half of pregnant Aboriginal women in South Australia are using the SA Aboriginal Family Birthing Program.** Philippa Middleton and Stephanie Brown (Murdoch Children's Research Institute) led an extensive evaluation of this program and discovered antenatal care attendance and health outcomes have improved. This innovative model of care addresses complex cultural, social and emotional wellbeing issues.
- > **Demonstrated that improved diet quality and exercise reduces the adverse risks for overweight and obese pregnant women and their infants.** Resulting from the LIMIT Study, Jodie Dodd and colleagues showed an 18% reduction in the risk of infants born weighing more than 4 kilograms.
- > **Demonstrated that mild exercise intervention in obese mice improves sperm function, restores embryo health, increases pregnancy rates and improves the metabolic health of offspring.** This discovery by Michelle Lane and colleagues contributes to the understanding of causes of infertility and weight disorders.
- > **Identified more than 1,000 genes that are expressed in the oviduct and regulated by the steroid hormone progesterone receptor transcription factor.** This work from Rebecca Robker and colleagues is important in understanding how progesterone prepares the oviduct to receive the oocyte for fertilisation and establishes the optimal environment for early embryo development and transport.
- > **Demonstrated that kidney health is related to early problems with blood vessels in teenagers who have diabetes.** This finding from an international trial by Jennifer Couper and colleagues, provides new treatment approaches for both diabetes and kidney complications.
- > **Improved support for large numbers of new mothers in South Australia through a combined nurse and internet-based program.** Michael Sawyer, John Lynch, Alyssa Sawyer and Kerrie Bowering partnered with the Women's and Children's Health Network to trial this project.
- > **Significantly progressed the development of algorithms to predict the risk of pregnancy complications.** Additionally, Claire Roberts and colleagues identified several gene environment interactions associated with this risk.

Financials

Categories

- NHMRC
- ARC
- Government and public sector
- Industry
- Donations and philanthropic foundations
- Robinson Research Institute foundations

The financial information presented is for Robinson Research Institute members only and may exclude some funds earned directly by members.



Funding highlights

During 2013 the Robinson Research Institute (RRI) continued to successfully attract funding from major bodies to support further work in research projects. A selection of highlights are summarised below.



NHMRC

The National Health and Medical Research Council awarded RRI members more than \$8.3 million for projects and fellowships commencing in 2014. Major project grants include:

\$763,953 to Professor Jozef Gecz

The role of UPF3B and nonsense mediated mRNA decay surveillance in the pathology of intellectual disability

\$755,934 to Professor Jodie Dodd

Causal pathways from maternal obesity to pregnancy, perinatal and childhood health outcomes

\$548,748 to Associate Professor Darryl Russell

Manipulating ovarian follicle–oocyte communication to control reproductive outcomes

\$534,021 to Professor Claire Roberts

Fetal sex: an important determinant of the placental transcriptome

\$511,226 to Dr Julia Pitcher

Mechanisms underlying impaired neuroplasticity in adolescents born preterm

\$499,169 to Dr Rebecca Robker

The obesity prone oocyte-causes, consequences, treatments

Australian Research Council (ARC)

Led by Professor Tanya Monro: Director of the Institute for Photonics and Advanced Sensing, Associate Professor Jeremy Thompson is a group leader in a \$23,000,000 ARC Centre of Excellence for Nanoscale BioPhotonics grant headquartered at the University of Adelaide.

The ARC awarded Professor Paul Thomas \$390,000 for the project: Genetic control of spermatogenesis - defining the role of SOX3 in spermatogonial progenitor cells.

Canadian Institutes of Health Research

Associate Professor Ros Haslam was awarded \$100,000 for the project commencing in 2013: Caffeine for apnea of prematurity.

Cancer Council SA and SAHMRI

Dr Carmela Ricciardelli was awarded \$93,981 for her Beat Cancer Project commencing in 2013: Hyaluronan – a marker and therapeutic target to overcome ovarian cancer chemoresistance.

Cerebral Palsy Foundation

Professor Jozef Gecz, Emeritus Professor Alastair MacLennan and Dr Clare van Eyk were awarded \$297,000 for their project commencing in 2014: Defining the role of genetic variations in cerebral palsy causation.

Channel 7 Children's Research Foundation

RRI members were awarded 13 project grants commencing in 2013/2014 totaling \$805,000 from the Channel 7 Children's Research Foundation. This includes \$75,000 for Associate Professor Cheryl Shoubridge's project: Preferential transmission of the mutant allele of the ARX homeobox gene.

Diabetes Australia Research Trust (DART)

DART awarded \$269,831 to RRI members in 2013 including \$149,831 to Dr Kathy Gatford for her project: Can exercise prevent diabetes in adults who grew poorly before birth? Studies in an ovine model of IUGR; \$60,000

to Professor Bill Hague for his project: MODY genotyping in a South Australian population of women with GDM; and \$60,000 to Associate Professor Leonie Heilbronn for her project: Effects of periodic fasting on the inflammatory profile in serum and adipose tissue.

Global Alliance for the Prevention of Prematurity and Stillbirth

An initiative of the Gates Foundation, Professor Sarah Robertson and colleagues were awarded \$1,500,000 for their project: Inflammatory pathways to preterm birth.

National Breast Cancer Foundation

Associate Professor Wendy Ingman and colleagues were awarded a \$200,000 Novel Concept Award for their project commencing in 2013: A novel concept for parity-induced breast cancer protection.

Ovarian Cancer Research Foundation

Professor Martin Oehler was awarded \$73,000 from the Ovarian Cancer Research Foundation (OCRF) to fund his study for: biospecimen collection and processing, maintenance of databases, and provision of samples for the OCRF tissue bank.

Tenix Foundation/Cerebral Palsy Alliance

Emeritus Professor Alastair MacLennan was awarded an \$800,000 Infrastructure Grant from the Tenix Foundation in 2013 to uncover the genetic causes of cerebral palsy.

Women's and Children's Hospital Foundation

The Women's and Children's Hospital Foundation awarded a total of \$419,619 to seven RRI members in 2013. This included \$53,462 to Dr Ann-Maree Vallence for her project: Neural and hormonal factors influencing consolidation of learning in children born preterm.



Fellowships and awards

ARC

ARC Future Fellow

Associate Professor Cheryl Shoubridge
(commenced 2013)

NHMRC

Commencing in 2013

Senior Research Fellowships

Associate Professor Vicki Clifton, Professor Jozef Gecz, Dr Michelle Lane and Associate Professor Mark Nottle

Career Development Fellowship

Dr Alice Rumbold

R.D. Wright Biomedical Career Development Fellowship

Dr Rebecca Robker

Awarded in 2013

Early Career Fellowship

Dr Rosalie Grivell and Dr Luke Grzeskowiak

Other fellowships

AADRF Postdoctoral Fellowship in Dementia

Dr Mitchell Goldsworthy (awarded 2013)

Endeavour Research Fellowship

Dr Ann-Maree Vallence (awarded 2013)

Australian Breast Cancer Research Postdoctoral Fellow

Dr Pallave Dasari (awarded 2013)

MS McLeod Postdoctoral Fellowship

Dr Martin Donnelley and Harsha Padmanabhan (awarded 2013)

Awards and prizes 2012

Adelaide Protein Group

Eiman Saleh awarded the Best PhD Oral Presentation

American Diabetes Association

Professor Caroline Crowther awarded the Norbert Freinkel Lecture Award for outstanding contribution to the understanding and treatment of diabetes in pregnancy

American Society for Reproductive Medicine

Professor Robert Norman awarded the Distinguished Researcher Award for outstanding contributions to research in reproduction

Asia Pacific Initiative on Reproduction

Professor Robert Norman awarded the 2013 Bayer Zydus Orator in India

Australia and New Zealand Society for Cell and Developmental Biology

Dr Sophie Wiszniak awarded the Best Oral Presentation at the South Australian State Meeting

Australian Government Department of Education

Dr Samuel Sidharta and Lachlan Frost awarded the Australian Postgraduate Award

Australian Institute of Policy and Science

Dr Lisa Moran awarded the 2013 South Australian Tall Poppy Award in the field of obesity, nutrition and women's health

Australian Society for Medical Research (ASMR)

Joshua Winderlich awarded the Best Poster Prize at the ASMR Annual Scientific Meeting

Left: Associate Professor Vicki Clifton; below: Dr Lisa Moran



Australasian Brain Stimulation Meeting

Dr Mitchell Goldsworthy awarded the Best Student Prize

Cardiac Society of Australia and New Zealand

Dr Dennis Wong awarded the Ralph Reader Award in the clinical research category

Endocrine Society of Australia

Hong Liu and Amy Woodridge awarded travel grants to attend the Endocrine Society of Australia's Annual Scientific Meeting

European Society for Human Reproduction and Embryology

Helana Shedadeh awarded the Best Scientific Paper prize

European Society for Reproductive Immunology

Professor Sarah Robertson awarded the Senior Researcher Award

International Pancreas and Islet Transplant Association

Mariea Bosco awarded the Young Investigator Award

Matrix Biology Society of Australia and New Zealand

Adrian Kaczmarek awarded the Dennis Lowther Award for the Best Student Poster

National Health and Medical Research Council

Dr Michael Gold and Associate Professor Helen Marshall were awarded one of the best 10 research projects of 2013 for their influenza infection in children research

Order of Australia

Professor Robert Norman for distinguished service to medicine in the field of reproductive health through contributions as a clinician and researcher

Perinatal Society of Australia and New Zealand

Dr Luke Grzeskowiak awarded the New Investigator Award at the national conference in Adelaide

Public Health Association of Australia

Associate Professor Helen Marshall awarded the National Public Health Association of Australia Fellowship in recognition of her contribution to public health

Robinson Research Institute

Professor Julie Owens awarded the Robinson Research Institute Director's Award

SA Science Excellence Awards

Dr Luke Grzeskowiak awarded the PhD Research Excellence Award

Society for Reproductive Biology

Professor Sarah Robertson selected to present the Founder's Lecturer, Dr Robert Gilchrist awarded Fellow of the Society for Reproductive Biology, and Sam Buckberry, Dr Loretta Chin, Katrina Copping, Jessica Miller, Nicole Palmer, Dulama Richani, Jacqueline Sudiman, Xuan Sun, Haman Wahid, Siew Wong and Bihong Zhang awarded Travel Awards

Society for the Study of Reproduction

Dr Hannah Brown awarded a Travel Award

Society of Hospital Pharmacists of Australia

Dr Luke Grzeskowiak awarded the Hospira Young Pharmacists Award and the PL Jeffs Early Career Pharmacist Award

Transplantation Society of Australia and New Zealand

Associate Professor Toby Coates awarded the Ian MacKenzie Prize for Outstanding Contribution to Transplantation, and Kisha Nandini Sivanathan, Dr Darling Rojas-Canales, Mariea Bosco and Chris Hope awarded a Young Investigator Award

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists

Professor Caroline Crowther selected to present the Ian McDonald Memorial Oration: *Evidently, Evidence in Obstetrics is Essential*

The University of Adelaide

Dr Lisa Akison, Jesia Berry, Dr Mitchell Goldsworthy, Dr Vicki Nisenblat and Dr Jimin Xiong awarded the Dean's Commendation for Doctoral Thesis Excellence

Dr Tim Baillie awarded the MH and MF Joyner Scholarship for Medicine and the Baillieu Supplementary Scholarship

Chris Hope awarded the Walter Dorothy Duncan Travel Grant

Noor Lokman awarded the Faculty of Health Science Vice Chancellor's Prize for Best Poster

Kisha Nandini Sivanathan awarded the Walter Dorothy Duncan Travel Grant

The University of South Australia

Victor Krawczyk awarded the Australian Postgraduate Award and Scholarship top-up
Ryan Green awarded a PhD Scholarship

Key collaborations

Hospitals

The Robinson Research Institute is firmly embedded within South Australia's public health system. Institute members occupy a physical presence and conduct collaborative research projects in the state's key hospitals, including the Women's and Children's, the Lyell McEwin, The Queen Elizabeth, Modbury and the Royal Adelaide.

The unique and diverse affiliations we enjoy in these institutions ensure our scientists and clinicians are integrated with South Australia's medical practice, play a role in shaping effective health policy and can access clinical material as appropriate.

Cook Medical

The Robinson Research Institute is at the core of an important collaborative relationship that exists between the University of Adelaide and Cook Medical, a world leader in the production of reproductive technologies and products.

One of the most successful of these is the Cook Medical Adelaide Fellowship. Other joint research projects focus on increasing the success of reproductive technologies.

Jean Hailes Foundation for Women's Health

The Robinson Research Institute collaborates with the Jean Hailes Foundation for Women's Health through the National Alliance on Polycystic Ovarian Syndrome (PCOS). This unique initiative brings together multidisciplinary clinicians, women with PCOS, researchers and government



representatives. The National Alliance on PCOS 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

The Robinson Research Institute collaborates with the University of Adelaide's Institute for Photonics and Advanced Sensing 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

Robinson Research Institute members have a key presence in clinical practice and research development at two leading fertility clinics in Adelaide: Repromed and Fertility SA.

Women's and Children's Health Research Alliance

The Robinson Research Institute has an active working relationship with the Women's and Children's Hospital, Women's and Children's Hospital Foundation, Women's and Children's Health Research Institute, Women's and Children's Health Network, SA Pathology, The South Australian Health and Medical Research Institute 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.

Fertility Coalition

The Robinson Research Institute is a founding partner in The Fertility Coalition, which was established in 2011 to launch the Your Fertility campaign. Additional partners include the Victorian Assisted Reproductive Treatment Authority (VARTA), Jean Hailes for Women's Health and Andrology Australia.

This ongoing campaign aims to provide accurate, evidence-based information about fertility to people who want to have children. The Coalition is supported by funding from the Australian Government Department of Health and Ageing under the Family Planning Grants Program. For more information visit yourfertility.org.au

South Australian Health and Medical Research Institute (SAHMRI)

The Robinson Research Institute collaborates with SAHMRI to partner in research relevant to the Healthy Mothers, Babies and Children research theme.

Universities

The Robinson Research Institute collaborates with many national and international universities and research institutes. We have trainee exchanges and co-funded grants with many of these, including those listed in the table below.

Institution	Country	Institution	Country
Baylor College of Medicine	USA	The University of Aberdeen	UK
Benaroya Research Institute	USA	The University of Alberta	Canada
Bristol University	UK	The University of Edinburgh	UK
Centres for Disease Control	USA	The University of Melbourne	Australia
Chungbuk National University	South Korea	The University of Nottingham	UK
ETH Zurich	Switzerland	The University of Queensland	Australia
Flinders University	Australia	The University of South Australia	Australia
Griffith University	Australia	The University of Tennessee	USA
Harvard Pilgrim Health Care Institute	USA	The University of Western Australia	Australia
Kings College London	UK	University of California, Los Angeles	USA
Kyushu University	Japan	Università degli Studi di Sassari	Italy
Liggins Institute	New Zealand	Universitätsspital Basel	Switzerland
LIMES Bonn	Germany	Université de Lausanne	Switzerland
London School of Hygiene and Tropical Medicine	UK	University College London	UK
McGill University	Canada	University of Buenos Aires	Argentina
Memorial Sloan Kettering Cancer Center	USA	University of Groningen	The Netherlands
Monash University	Australia	University of New South Wales	Australia
MRC National Institute for Medical Research	UK	University of North Carolina	USA
Oxford University	UK	University of Pennsylvania	USA
Prince Henry's Institute for Medical Research	Australia	University of South Hampton	USA
Queensland University of Technology	Australia	University of Würzburg	Germany
Samson Institute for Health Research	Australia	Victoria University	Australia
São Paulo State University	Brazil	Victoria University of Wellington	New Zealand
South Australian Research and Development Institute	Australia	Vrije Universiteit Brussel	Belgium
The Florey Institute of Neuroscience and Mental Health	Australia	Washington State University	USA
		Westmead Millennium Institute for Medical Research	Australia



Presentations and speaker invitations

In 2013 Robinson Research Institute members were invited to deliver more than 200 presentations in Australia and around the world.



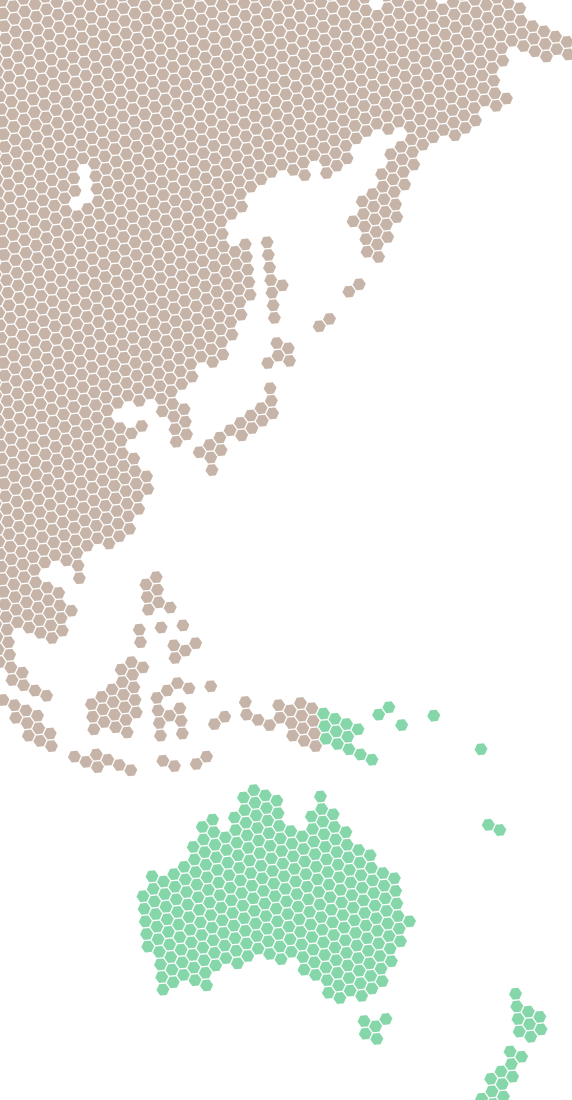
International Visitors

The Robinson Research Institute welcomed many distinguished international researchers and students for collaboration, conferences, seminars and exchange programs throughout 2013.

These interactions provided the opportunity to share research, knowledge and expertise, and the Institute will continue to foster international collaborations throughout 2014.

Visitor	Affiliation	Country
Prof Akifumi Akamine	Kyushu University	Japan
Prof Richard Anderson	The University of Edinburgh	UK
Dr John Bromfield	University of Missouri	USA
Dr Bert de Vries	Radboud University	Netherlands
Prof Duska Dragun	Charité - Universitätsmedizin	Germany
Prof Dan Geschwind	UCLA	USA
Prof Vincent Hascall	Cleveland Clinic Lerner Research Institute	USA
Dr Vera Kalscheuer	Max Planck Institute for Molecular Genetics	Germany
Prof Naomi Kashiwazaki	Azabu University	Japan
Dr Bruce Lessey	University of California, San Diego	USA
Dr Mariana Fernandes Marchardo	Sao Paulo State University	Brazil
Dr Maria P Miano	Consiglio Nazionale delle Ricerche	Italy

Visitor	Affiliation	Country
Mr Kawazoe Nobuyuki	Kyushu University	Japan
Prof Kazuaki Nokama	Kyushu University	Japan
Dr Maria Passafarro	Telethon Institute of Genetics and Medicine	Italy
Prof Anna Plaas	Tobias Rush: University of Dayton	USA
Dr Cris Print	The University of Auckland	NZ
Prof John C Rothwell	University College London	UK
Ms Anika Ruhl	Graduate School of Life Sciences	Germany
Prof John Sandy	Tobias Rush: University of Dayton	USA
Dr Atushi Tomokiyo	Kyushu University	Japan
Prof Dietmar Vestweber	Max Planck Institute for Molecular Biomedicine	Germany
Prof Miles Wilkinson	University of California, San Diego	USA
Prof Gregory Zimet	Indiana University School of Medicine	USA



Community engagement

From Bench to Bedside – the Story of the Robinson Research Institute (1958 – 2013)

From Bench to Bedside is a video commissioned by Professor Rob Norman before he stepped down as Director in September 2013. It features some of the Institute's most prominent researchers and clinicians, and captures the history of world-leading discoveries and advances, which have emerged from the University of Adelaide's Obstetrics and Gynaecology Department over the last fifty years.

The video celebrates the dedication and passion of key people, and demonstrates how a strong culture of collaboration between science and medicine is vital for research excellence and transition into clinical practice.

Visit the Robinson Research Institute website to watch the Story.
adelaide.edu.au/robinson-research-institute/about/history/

Your Fertility

Since 2011, Your Fertility has worked to address the gap in community knowledge and understanding about modifiable factors that affect fertility, to prevent involuntary infertility. By sharing the latest information, Your Fertility aims to empower people to make informed and timely decisions regarding their reproductive health.

Delivered by the Fertility Coalition consisting of the Robinson Research Institute, the Victorian Assisted Reproductive Treatment Authority, Jean Hailes for Women's Health and Andrology Australia, Your Fertility reached over two million Australians through the web, social media, advertising and traditional media in 2013.

As a partner, the Robinson Research Institute made important contributions to the program and its major activities, including:

Fertility Week (2-8 September)

Fertility Week aims to promote conversations between individuals and health professionals. In 2013, fertility experts from the Institute ran the seminar: It's time for Your Fertility – age, weight, smoking, alcohol, timing.

'Fertility is ageist' campaign

Focus groups run by the Fertility Coalition revealed several common misconceptions about fertility, particularly about the impact of age on fertility.

"The misconception that you can have a healthy child at any age may have emerged from comforting messages that don't take into account biological reality and the latest research," argues Professor Sarah Robertson, Director.

"There is the view that good health will 'trump' a woman's age. While good health will help with conception and having a healthy baby, the age of both women and men is the single biggest factor affecting fertility and reproductive health outcomes."

For more information visit yourfertility.org.au

PSANZ Satellite Meeting: Early Life Programming and Health Outcomes

As part of the Perinatal Society of Australia and New Zealand (PSANZ) Annual Congress, the Robinson Research Institute hosted a satellite meeting on Early Life Programming and Health Outcomes in April 2013.

Attended by more than 70 people, the meeting featured 16 internationally distinguished experts in reproductive and paediatric health research, and was attended by senior and emerging researchers, clinicians, community health employees, physicians in training, and nurses.

The meeting was highly successful and demonstrated that health professionals desire access to the latest research outcomes to translate into practice.

The program was divided into four sessions and concluded with a panel discussion made up of researchers, clinicians and health employees.

This meeting enabled attendees to share research outcomes, discuss new directions and to foster collaborative opportunities.

Healthy Development Adelaide

Healthy Development Adelaide (HDA) plays a key role in South Australia linking research, service delivery and policy development. Through these linkages HDA promotes, facilitates and enables multidisciplinary research that advances understanding of healthy development and ensures the physical, psychological and social health of infants, children and adolescents.

HDA was established in 2004 as an initiative of the University of Adelaide, and is currently led by Professor Claire Roberts (Robinson Research Institute, University of Adelaide) and Professor Michael Sawyer (Women's and Children's Health Network / Robinson Research Institute, University of Adelaide).

In 2013, HDA was supported by a partnership of South Australian organisations, including the Robinson Research Institute, Channel 7 Children's Research Foundation, University of South Australia, Flinders University, Department for Education and Child Development, Fertility SA, Repromed, Women's and Children's Health Research Institute and Flinders Fertility.

HDA has over 230 Research Members and 320 Associate Members drawn from universities, local, national and international institutions, government and the general community.

For more information visit adelaide.edu.au/hda

HDA events

HDA events create opportunities for communication, networking and multidisciplinary research collaborations. The events are held throughout the year and are well attended by a broad array of researchers, students, government, health service personnel, educators, organisations, teachers and the general community. During 2013, 12 events were held with more than 1,200 attendees.

HDA promotes, facilitates and enables multidisciplinary research.



2013 events

9th annual HDA Oration

> Can we change the environment to prevent diabetes in childhood? August

The evening was chaired by HDA Co-Convenor Professor Michael Sawyer who presented Professor Jennifer Couper, Head of the Diabetes Group, with the 2013 Healthy Development Award for excellence in research contributing to healthy development.

HDA Thematic Evenings

These research evenings include four multidisciplinary speakers and are designed to bring like-minded people from different areas and organisations together for a common theme. Three HDA Thematic Evenings were held in 2013:

> Family Connections: making the bonds stronger, April

> Preconception Care: planning is paramount, May

> Making a better future for our kids, July

HDA Collaborative Events

> Play Your Part: protecting children is everybody's business, September

With the Australian Centre for Child Protection, University of South Australia, and the National Association for Prevention of Child Abuse and Neglect, this forum was held during National Child Protection Week.

> It's Time for Your Fertility, September

With the Robinson Research Institute, University of Adelaide and Your Fertility, this event was held during Fertility Week.

> Scientific Networking Evening, June

With the Australian Society for Medical Research (ASMR – SA Branch).



1. Born Too Soon event

2. Professor Jennifer Couper accepting her award from Professor Michael Sawyer (left) and Professor Claire Roberts (right) at the 9th annual HDA Oration

3. (L-R) Professor Maria Makrides, Dr Carmel Collins, Professor Jodie Dodd, Amanda Blair (MC), Professor Claire Roberts, Professor Sarah Robertson and A/ Professor Debbie Palmer at the Early Life Nutrition event

> Early Life Nutrition, October

With the FOODplus Research Centre incorporating the CRE Foods for Future Australians, the Robinson Research Institute, University of Adelaide and the Women's and Children's Health Research Institute (WCHRI).

> Development and experience of the Middle Development Instrument in Canada and piloting in South Australia, November

With the Fraser Mustard Centre, a collaboration between the Department for Education and Child Development and the Telethon Institute for Child Health Research.

HDA Career Development Events

Two HDA Career Development events were held in 2013. These events offer students and early career researchers the opportunity to network and further their career development.

> Ethics in Research: contemporary issues and your responsibilities, September

> Health Sciences: establishing your research career, October

Research Symposium

In November 2013, the Robinson Research Institute Symposium was held at the National Wine Centre in Adelaide. In its second year, the full day event provided the opportunity for researchers and professionals to come together to network, and learn more about the great research being undertaken across the Institute.

The program was segmented into research surrounding the Institute's four themes: Fertility and Conception, Pregnancy and Birth, Early Origins of Health, and Child and Adolescent Health. The audience experienced exciting research presentations from senior, mid and early career researchers, insights into clinical and professional roles, a poster competition and awards presentation.

In addition, Honours student Laura Spencer shared her personal and moving account of giving birth to her daughter Heidi at just 25 weeks gestation. Laura's experience inspired her to take up research in an effort to help uncover the causes of preterm birth, and to reduce the occurrence of other parents experiencing a similar journey.

The event concluded with an awards presentation. Congratulations to John Schjenken and Nicole McPherson for winning the poster display competition.

The Robinson Research Institute Directors Award was presented to Professor Julie Owens for her outstanding research and commitment to the establishment and future direction of the Institute.

The Jeffrey Robinson Scholarship was awarded to Zuleeza Ahmad, an outstanding student who is interested in placental growth and plasticity of insulin secretion.



Top: Macarena Bermudez Gonzalez, Laura Watson, Astrud Tuck and Sam Buckberry
Bottom: Rachel Kontic, Prof Julie Owens, Prof Sarah Robertson and Prof Rob Norman

Research Tuesdays: Pregnant Pause

In its eighth year, Research Tuesdays lectures are designed to share the breadth and depth of the University of Adelaide's research with the community.

Professor Michael Davies, Head of the Robinson Research Institute's Life Course and Intergenerational Health Group, was selected to present in August 2013 on the topic Pregnant Pause.

Held in the University's new Bragg's Lecture Theatre and watched by 120 attendees, Michael's presentation explored important new questions emerging from life-creating infertility treatment.

Around 5 million individuals have been born as a result of assisted reproductive technology. In his presentation, Michael highlighted the questions now being asked about the effectiveness, and long-term social and biological consequences to mother and child.

Hon Jack Snelling, Minister for Health and Ageing visits the Robinson Research Institute

In August 2013, the Institute was pleased to welcome the Hon Jack Snelling, Minister for Health and Ageing, when he visited the North Adelaide site.

The visit provided the opportunity to discuss the Institute's research agenda and to highlight the importance of health research at the earliest stages of life.

The Minister toured the North Adelaide and Medical School facilities and laboratories. He met with Institute Clinicians and Research Leaders to learn more about the work of the Institute and South Australia's leadership and excellence in reproduction, pregnancy and child health.

Society for Reproductive Biology Sponsorship

The Robinson Research Institute was proud to again support the Society for Reproductive Biology (SRB) by sponsoring the Robinson Research Mid-Career Award, awarded to Professor Justin St John in 2013.

The award was presented at the Annual Scientific Meeting of the Endocrine Society of Australia and the Society for Reproductive Biology at the Sydney Convention Centre in August. This is a prestigious award valued at \$3,000 and recognises sustained and substantial research achievement in the field of reproductive biology, for a researcher who is less than 15 years post-receipt of their Doctorate.

The Society for Reproductive Biology is the premier scientific society for reproductive biology in the Asia-Pacific region. The Institute has a long-standing relationship with SRB and 2013 was the 8th year of our partnership. The Institute will again sponsor this award in 2014, 2015 and 2016.



Science Stories

Science stories is a bi-monthly publication designed to capture personal anecdotes and provide an insight into the life of a scientist and/or clinician, who is active in research through one or more of the Institutes four themes - Fertility and Conception, Pregnancy and Birth, Early Origins of Health, and Child and Adolescent Health.

The stories are targeted to both a scientific and lay audience. The Institute will continue to grow Science Stories in 2014.

Visit the link below to read Science Stories:
adelaide.edu.au/robinson-research-institute/researchers/science-stories/

In 2013 the Robinson Research Institute released 6 editions of Science Stories:

Born Too Soon

Preterm birth is a global health challenge. 15 million babies are born preterm each year, with 24,000 born here in Australia. Babies born too soon are at increased risk of respiratory, gastrointestinal and neurological problems, and in some cases these can persist over the course of their life.

The Institute plays a key role in educating the community on the health issues related to preterm birth, and in doing so, we aim to reduce the high rate of babies born early.

In an effort to raise awareness and increase knowledge across society, the Institute collaborated with Healthy Development Adelaide in November 2013 to host a community forum on the topic Born Too Soon.

Convened by Institute Director Prof Sarah Robertson, the audience was treated to three inspiring presentations by Research Leaders with expertise in preterm birth research:

- > A/Prof Michael Stark explained that treatment no longer focuses on survival alone, but on optimal survival, free from significant morbidity
- > Prof Claire Roberts discussed the known risks associated with preterm delivery, including the factors that can be modified to reduce the risk
- > Dr Julia Pitcher described how interactions between abnormal cortical development and the early postnatal environment affect learning and memory in adolescents born preterm

In addition, Honours student Laura Spencer shared her personal and moving account of giving birth to her daughter Heidi at just 25 weeks gestation. Laura's experience inspired her to take up research in an effort to help uncover the causes of preterm birth, and to reduce the occurrence of other parents experiencing a similar journey.

162 people from the community and professionals working in the area attended the forum. The event was informative and provided an excellent opportunity to share knowledge, and explore ideas for future collaborations.



New cell discovery reveals secrets of ovarian development
 Prof Ray Rodgers



Caring for very sick babies: how can we know when to let them go?
 A/Prof Dominic Wilkinson



Vaccination against chicken pox reduces severe illness and death in Australian children
 A/Prof Helen Marshall



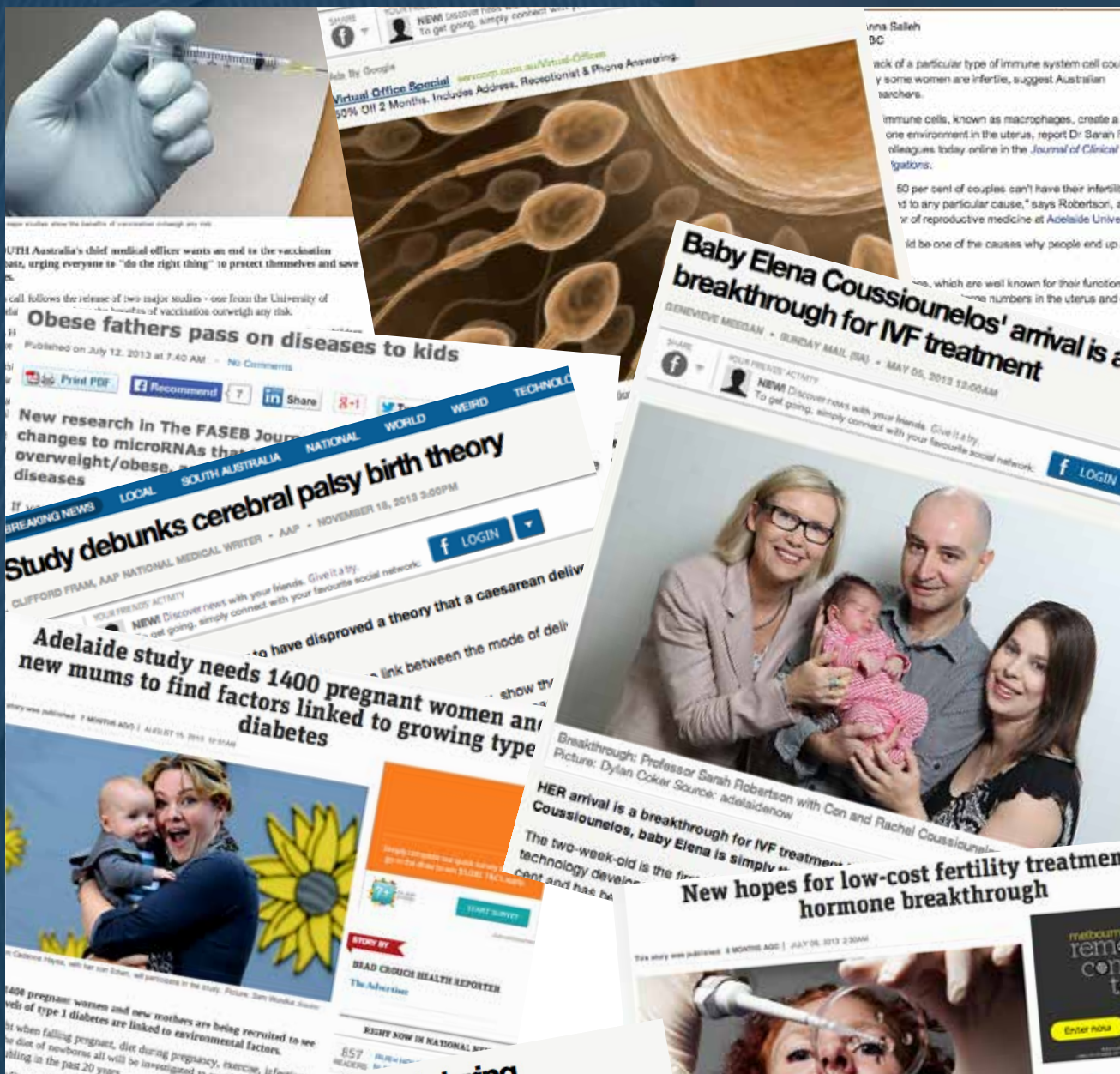
Longer not always better in twin pregnancies
 Prof Jodie Dodd



Exciting new target for schizophrenia diagnosis and treatment
 Dr Quenten Schwarz



Quality control in protein production ensures normal brain development
 Prof Jozef Geacz



Media impact

The Robinson Research Institute continues to make a strong impact in the media. In 2013, the Institute reached more than 19 million people.

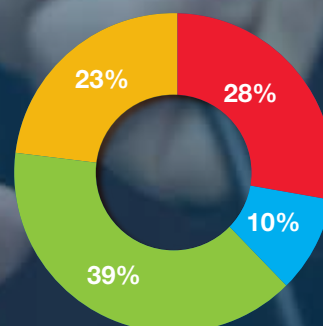
The Institute actively publicises its research in the media to better inform the community about advances in fertility, pregnancy and child health issues.

The Institute will continue to engage the media in 2014 to share its discoveries, and increasingly will utilise social media for communication and conversations between researchers and the community.

Follow the Robinson Research Institute

-  facebook.com/RobsInstitute
-  twitter.com/RobsInstitute
-  youtube.com/user/RobinsonInstitute

Media Type	Audience/circulation
Internet	5,432,147
Radio	2,020,500
Press	7,456,923
Television	4,490,000





Group highlights

Groups aligned to themes



Fertility and Conception

Breast Biology and Cancer
led by A/Prof Wendy Ingman | 46

Comparative Reproduction
Biology of Mammals
led by Prof Bill Breed | 29

Early Development
led by A/Prof Jeremy Thompson | 66

Endometriosis
led by Dr Louise Hull | 44

Gamete and Embryo Biology
led by Dr Michelle Lane | 50

Mammalian Reproduction
led by A/Prof Frank Grutzner | 41

Metabolism and Health
led by A/Prof Leonie Heilbronn | 43

Neural Development
led by Prof Paul Thomas | 65

Ovarian and Reproductive Cancer Cell Biology
led by A/Prof Darryl Russell | 62

Ovarian Cell Biology
led by Dr Rebecca Robker | 60

Ovarian Developmental Biology
led by Prof Ray Rodgers | 61

Reproductive and Peri-conceptual Medicine,
led by Prof Rob Norman | 52

Reproductive Biotechnology
led by A/Prof Mark Nottle | 52

Reproductive Cancer,
led by Prof Martin Oehler & Dr Carmela Ricciardelli | 53

Reproductive Immunology
led by Prof Sarah Robertson | 59



Pregnancy and Birth

Cerebral Palsy
led by E/Prof Alastair MacLennan | 50

Epigenetics & Genetics
led by Prof Stefan Hiendleder | 44

Health of Pregnant Mothers and Babies
led by Prof Jodie Dodd | 35

Health of Women and Babies
led by Prof Caroline Crowther and
Ms Philippa Middleton | 33

Obstetric Medicine Research
led by Prof Bill Hague | 42

Placental Development
led by Prof Claire Roberts and Prof Gus Dekker | 58

Pregnancy and Development
led by A/Prof Vicki Clifton | 30



Early Origins of Health

Circadian Physiology
led by Prof David Kennaway | 47

Early Origins of Health and Disease
led by Prof Julie Owens | 55

Life Course & Intergenerational Health
led by Prof Michael Davies and
Prof Vivienne Moore | 34

Neonatal Medicine Research
led by A/Prof Michael Stark | 65

Neuromotor Plasticity and Development
led by Dr Julia Pitcher and A/Prof Michael Ridding | 57



Child and Adolescent Health

Allergy & Vaccine Safety
led by A/Prof Michael Gold | 39

Cystic Fibrosis
led by A/Prof David Parsons | 56

Developmental and Genetic Immunology
led by Prof Antonio Ferrante | 36

Diabetes
led by Prof Jenny Couper | 32

Gastroenterology
led by A/Prof Taher Omari | 54

Molecular Immunology
led by A/Prof Simon Barry | 27

Molecular Neurogenetics
led by A/Prof Cheryl Shoubridge | 64

Neurogenetics
led by Prof Jozef Gecz | 37

Research and Evaluation
led by Prof Michael Sawyer | 62

Sleep Disorders
led by Prof Declan Kennedy | 48

Transplantation Research
led by Prof Toby Coates | 31

Vaccines and Immunisation
led by A/Prof Helen Marshall | 51

Associate Professor Simon Barry

Molecular Immunology

Understanding the molecular basis for immune tolerance

How does a healthy immune system balance a swift response to fight off pathogens with maintaining a tolerance to harmless challenges such as food and normal body tissues? A subset of immune cells known as regulatory T cells (Tregs) is believed to play a critical role in determining such outcomes. Tregs are essential for immune tolerance, and defects in this particular cell population are implicated in autoimmune disorders, cancer and other diseases. Simon's group conducts research to understand and characterise Tregs under normal conditions, with a view to understand what goes wrong with these cells in immunological disorders.

Simon's group uses state of the art molecular biology to investigate all the genes involved in immune function in Tregs, and to understand how the key genes are regulated in a coordinated way to control the normal function of the Treg cell. The researchers then compare this with cells from patients to pinpoint the places where functional fitness or potency is lost, so that they can devise better strategies to diagnose and treat the diseases.

The group investigates the way that genes are switched on and off to control T cell function. They have focused on a master switch gene, or transcription factor, named FOXP3, which orchestrates the function of Treg cells. Simon's group are teasing apart the networks of gene regulation. They are investigating the role of microRNAs in shaping function in healthy Tregs as well as attempting to develop better tools for identifying and handling the Treg cells. The researchers have identified a novel biomarker on human Treg cells, named PI16, and are now testing its capacity to: (a) identify stable Tregs and/or (b) be a diagnostic tool for loss of Treg function in disease. Additionally, the group are developing a Treg cell therapy intended to reset or redirect the immune system to prevent autoimmune disease, or to prevent transplant rejection.

The group plans to take its novel molecular tools into clinical samples where immune tolerance has broken down so that the precise points where function has altered can be identified. With this knowledge, they aim to develop biomarkers, drug targets and cell therapies for diagnosis and treatment of these diseases.



Group members

Research fellows: Timothy Sadlon and Cheryl Brown

Research assistants: Grace Ang, Susan Bresatz, Sonia Dayan, Batjargal Gundsambuu and Tzu Ying Yap

PhD candidate: Kristen Malatesa, Natasha McInnes, Arunesh Mohandas, Steve Pederson and John Welch

International collaborators: Marc Beyer, Thomas Duhon, Giovanna Lombardi, Joachim Schultze, Tim Tree and Kathryn Wood

National collaborators: Greg Goodall, Tom Gonda, Raymond Steptoe, Nico Voelcker

Professor Mark Bartold

Periodontal Repair

Using mesenchymal stem cells to regenerate structures affected by periodontal disease

Periodontitis is one of the most common chronic inflammatory conditions with up to 60% of the population experiencing it in some form. This inflammatory condition results in destruction of the tooth supporting tissues and, when left untreated, can lead to tooth loss.

The Periodontal Repair Group is investigating engineering mesenchymal stem cells from the periodontal tissues to repair damage caused by periodontitis.

The researchers have successfully used allogeneic periodontal mesenchymal stem cells to repair periodontal defects in an ovine model of periodontitis. They have also generated induced pluripotent stem cells (iPS) from periodontal cells. These iPS cells have been differentiated into periodontal mesenchymal-like stem cells in preparation to test them for their regenerative capacity.

Mark's group will continue to utilise iPS cells for periodontal regeneration using a variety of tissue engineering approaches.



Group members

Research leaders: Mark Bartold, Stan Gronthos

Postdoctoral researchers: Kim Hynes, Danijela Menicanin, Atsushi Tomokiyo

Laboratory manager: Victor Marino

Research assistant: Jia Ng

Senior lecturer: Peter Zilm

Collaborators: Dietmar Huttmacher, Saso Ivanovski and Naohisa Wada



Group members

Senior scientist: Lisa Ebert

Postdoctoral researchers: David Dimasi and Lachlan Moldenhauer

PhD candidates: Kate Parham and Wai Sun

Honours student: Prithi Sacchi

Research assistants: Michaelia Cockshell and Emma Thompson

Technician: Samantha Escarbe

Research trainee: Lih Tan

Affiliate members: Claudine Bonder and Lisa Ebert

Collaborators: Toby Coates, Michael Hickey, Claire Jessup, Stuart Pitson, Angel Lopez and Gibor Tyigi

Associate Professor Claudine Bonder

Vascular Biology Laboratory

Understanding vascular biology in disease

Delivery of blood occurs via an intricate network of vessels distributed throughout the body. Blood vessels are key to tissue regeneration but also contribute the progression of diseases such as cancer and cardiovascular disease.

Improved understanding of how blood vessels form will provide new therapeutic opportunities and increase public health. The Vascular Biology Laboratory focuses on endothelial cells (ECs), which line the lumen of all blood vessels and thus play a pivotal role in normal and disease states.

This group have three main areas of interest:

1. During allergic inflammation, ECs regulate leukocyte recruitment via adhesion molecule expression – the group are interrogating this process with an aim to block neutrophil recruitment and attenuate allergic inflammation
2. Endothelial progenitor cells (EPCs) directly contribute to blood vessel formation (vasculogenesis) in the pathological settings of cardiovascular disease, cancer and organ transplantation. The group recently identified a new sub-population of EPCs and are now interrogating these cells to identify new targets for therapeutic application.
3. Breast cancer and melanoma progress via a process called vasculogenic mimicry. This is a process wherein cancer cells form vascular-like structures to provide access to the blood supply for nutrients and oxygen. The group are investigating the processes by which vasculogenic mimicry occurs and are defining targets to prevent cancer progression.

“Developing these studies may provide new treatment options for cancer.”

In 2013 the group made significant developments in their focus areas of allergic inflammation, EPCs and vasculogenic mimicry. They identified that sphingosine kinase-1 and sphingosine-1-phosphate are key to the recruitment of neutrophils during allergic inflammation and have begun to examine a new treatment option for allergy sufferers. Their EPC work has been recognised by the Australian government via a new six-year \$59 million Co-operative Research Centre titled ‘Cell Therapy Manufacturing’. In this work, new biomaterials will be manufactured to bind human EPCs together with human islets for increased cure rates of patients with type-1 diabetes. This work is in collaboration with Professor Toby Coates and the biomaterial group at the University of South Australia. Finally, in close collaboration with Dr Lisa Ebert and Professor Angel Lopez, the group has identified key molecules that drive vasculogenic mimicry in melanoma and breast cancer. Developing these studies may provide new treatment options for cancer.

Professor Bill Breed

Comparative Reproduction Biology of Mammals

Determination of the health status and reproductive biology of local native mammals

The Comparative Reproduction Biology of Mammals Group is investigating the basic biology of the native mammals of Australia with a focus on their reproductive biology and its application to the conservation of these species. This knowledge should assist in maintaining viable populations of the local native mammalian species. The group's work includes studies on hairy-nosed wombats, koalas, bilbies and several species of native rodents. The group are particularly interested in the species' reproductive biology, the ways the species have adapted to the environments in which they occur, and the direct and indirect threats posed to these populations by humans.

Recently the group have focused on investigating two pathologies of local marsupials - kidney disease in the koala population and sarcoptic mange in hairy-nosed wombats. Other research has focused on the morphological and molecular evolution of sperm and eggs and their interaction at fertilisation.

Bill, in collaboration with Dr Natasha Speight, published results on renal failure in the local koalas showing that some of the individuals have renal insufficiency and dysfunction due to oxalate nephrosis with the accumulation of calcium oxalate crystals occurring in the kidneys. In collaboration with Dr Laura Ruykys, Bill investigated the occurrence of sarcoptic mange in a hairy-nosed wombat population in the Riverland and found these animals had elevated white blood cell counts but depressed haematocrit and creatinine values in their peripheral blood with hyperplasia and hyperkeratosis of the dermis of the skin being evident. Administration of ivermectin to a few individuals appeared to increase their chances of survival.

For the reproductive biological studies, the group have recently determined the optimal cryopreservation procedures for spermatozoa in two native rodent species.



“ The group’s work includes studies on hairy-nosed wombats, koalas, bilbies and several species of native rodent. ”

They have also continued to investigate sperm-egg interactions at the time of fertilisation and found that the unique cytoskeletal processes on the sperm head of most of the old endemic rodents are involved in enhancing the binding of the spermatozoon to the extracellular coat around the egg, the zona pellucida, at the time of the acrosome reaction.

By comparing reproductive processes in different mammals, we can learn a lot about which important events have been retained through evolution, and gain insight relevant to human biology.



Group members

Research assistant: Chris Leigh

PhD candidate: Natasha Speight

Honours students: Katherine Ferres and Yu Wang

Collaborators: Laura Ruykys, Dave Taggart, Eleanor Peirce, Michelle Lane, and Hassan Bakos



Associate Professor Vicki Clifton

Pregnancy and Development

Improving the health of pregnant women and their babies in socially disadvantaged communities

Group members

Postdoctoral researcher:
Annette Osei-Kumah

Academic: Annette Osei-Kumah

Emeritus member: Basil Hetzel

Senior postdoctoral researcher:
Dianne Rodger

Research fellows: Jessica Grieger, Luke Grzeskowiak, Zarqa Saif and Astrud Tuck

Research midwife: Karen Rivers

Research midwife/Masters candidate: Julia Dalton

Research nurse: Kate Roberts-Thomson

PhD candidates: Natalie Aboustate, Maureen Busutti, Isabella Rose-Meredith, Julie Tucker, Amy Wooldridge, Ian Wright, Yann Chow and Nurul Zainal

Technical officer: Jessica Forrest

Administrative assistant: Kelly Fulton

Affiliate members: Jon Hirst, Nayana Parange, Karen Moritz, Vanessa Murphy, Roger Smith and Lisa Wood

Collaborators: Margaret Arstall, Justin Beilby, Robert Bischof, Jeff Bowden, Robert Bryce, Tim Cole, Alexandre Francois, Peter Fuller, Peter Hoffman, Sal Humphreys, Yoga Kandasamy, Jonathan Karnon, Alison Kitson, Tanya Monro, Janna Morrison, Tim Moss, Elizabeth Murphy, Susan Prescott, Anil Roy, Richard Ruffin, Richard Saffery, Andrew Skuse, Brian Smith, Andrew Tai, Michael Wilmore and Anne Wilson

Many pre-existing diseases that affect the health of the mother and the development of her baby can complicate pregnancy. Asthma is a highly prevalent disease in Australian women that is associated with poor outcomes for the baby including preterm delivery, stillbirth and growth restriction. These outcomes can be reduced if asthma is managed effectively during pregnancy.

The Pregnancy and Development Group are taking a multi-layered approach towards better understanding asthma during pregnancy including its impact on mother and baby. They examine clinical questions associated with improving health service, health education and communication, and asthma management, as well as basic scientific questions associated with understanding the mechanisms that affect fetal development and the long-term health of the children of mothers with asthma.

The group's research involves recruiting pregnant women at their first antenatal visit and following them throughout gestation and post partum to determine the events that contribute to the health of the child. The group examines a number of questions related to maternal diet, asthma control, health knowledge, literacy, and communication.

In addition, the group is examining children for cardiovascular health, growth, neuro-development and immune development, and finding links to in-utero events.

In 2013 the group progressed a diverse research program, including examining how maternal diet and asthma affects perinatal outcomes. An interesting association they found was that maternal high fat and sugar intake pre-pregnancy was linked to an increased risk of preterm birth.

The group is now focused on evaluating the benefits of improving dietary intake in a population of asthmatic women from a socially disadvantaged community in Northern Adelaide.



Professor Toby Coates

Transplantation Research

Developing novel cell based therapies to treat organ failure and provide immunosuppression

Organ transplants are one of the major triumphs of modern medicine but they are plagued with the side effects of associated immunosuppressive drug therapy, which damages their function and longevity. The Transplantation Research Group seeks to use different cell types as transplant therapy to:

- > Replace function (islet cells to treat type-1 diabetes)
- > Repair blood supply to transplanted organs (endothelial progenitor cells)
- > Induce immunosuppression without drugs (mesenchymal stem cells and dendritic cells)

In 2013 the group was successful in its application to become a component of the Cooperative Research Centre for Cell Therapy Manufacturing – a \$59 million investment of funds from the Australian Federal Government and the Industry coordinated through the University of South Australia based at Mawson Lakes. This funding was one of three (out of 15 proposals) that were funded and was announced by the then Prime Minister, Julia Gillard in January 2013.

The South Australian and Northern Territory Islet Program (SANTIP) were also awarded National Funded Centre status to provide clinical islet transplantation for the benefit of Australians with type-1 diabetes. The award of South Australia's first Nationally Funded Centre for Islet Transplantation was another highly significant milestone for the translational clinical research performed in the group. The Nationally Funded Centres program exists to fund high cost low volume clinical procedures for the benefit of all Australians and recognises the excellence in cell therapy developed through the research group.

The group is now focusing on translating research into clinical islet transplantation devices in the transplant clinic.



Group members

PhD candidates: Mariea Bosco, Bron Lett, Ernesto Hurtado Perez, Nitesh Rao and Kisha Sivanathan

Clinical researchers: Rob Carroll, Randall Faull, Shilpa Jesudason and Chen Au Peh

Senior scientists: Christopher Drogemuller, Sveltana Kireta and Daniella Penko

Technical officer: Julie Johnston

Senior postdoctoral researchers: Claudine Bonder, Shane Grey and Plinio Hurtado

Postdoctoral researcher: Darling Rojas-Canales

Senior scientists: Chris Hope and Jodie Nitschke

Honours students: Alexander Fuss, Peter Rose and Sebastian Stead

Masters student: Fredrick Chia



Group members

Clinical researcher: Alexia Pena

Research coordinator: Megan Penno

Research fellows: Simon Barry and Oana Maftei

PhD candidates: Jemma Anderson and Shiree Perano

Research nurse: Sarah Beresford and Meredith Krieg

Sonographer: Roger Gent

Collaborators: ME Craig, LC Harrison and TW Jones

Professor Jenny Couper

Diabetes

Preventing type-1 diabetes and its complications in young people

The incidence of type-1 diabetes in childhood has increased worldwide and has doubled in Australia over the last 20 years. This suggests the importance of changing environmental factors in its development. If we can identify the environmental triggers we will have a way of intervening to restore a healthy immune system in the body to prevent diabetes. Children with type-1 diabetes have an increased lifetime risk of heart, kidney and eye disease due to the effect of the diabetes on their blood vessels. These first subtle changes can be detected from adolescence, when they are still at a reversible stage. Therefore prevention and intervention during childhood is very important.

The Diabetes Group conducts clinical and laboratory research which focuses on:

- > The environmental exposures that drive the development of type-1 diabetes
- > Immune regulatory function in type-1 diabetes
- > Treatment innovations to protect blood vessel health of children and adolescents who have type-1 diabetes

The group is also the Australian centre for ultrasound measurement of vascular health for the international AdDIT trial (Adolescent type-1 diabetes Cardio-Renal Intervention Trial).

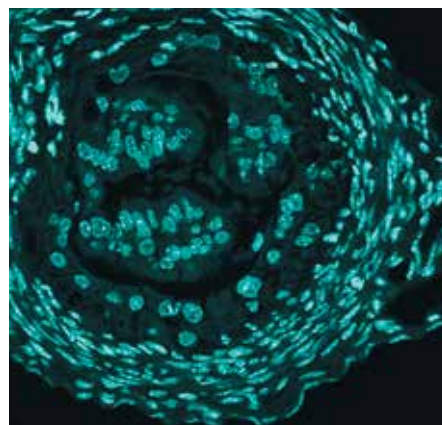
In 2013, the group began a nationwide cohort study from pregnancy to determine how the modern environment drives the development of type-1 diabetes, ENDIA. In conjunction, there were studies of immune regulatory function in preclinical and recent onset type-1 diabetes. Researchers continued two randomised controlled trials. The first is assessing the benefits of metformin in preserving vascular health in adolescents with type-1 diabetes as well as strategies to help blood glucose control in children with cystic fibrosis. The group leads the South Australian arm of international trials aimed at preventing type-1 diabetes using immune tolerance strategies and preventing vascular complications in

adolescents. In 2013 researchers completed follow up of a longitudinal cohort of South Australian children including healthy children, obese children and children with type-1 diabetes to assess the value of ultrasound for measuring blood vessel changes in early cardiovascular disease.

Group Director, Jenny Couper is on the steering committee of the Juvenile Diabetes Research Foundation (JDRF) Clinical Research Network and is appointed to the JDRF International Microbiome Consortium, JDRF Scientific Review Panel, and is a Chapter Editor for ISPAD (International Society of Pediatric and Adolescent Diabetes) guidelines. Dr Alexia Pena is on the writing group for the International Guidelines for polycystic ovary disease in adolescents and is the Australasian Paediatric Endocrine Group secretary.

In 2014, the group has two primary research focuses:

- > To continue recruitment of 1,400 pregnant women to unravel the effects of genes, environment and the microbiome on the development of type-1 diabetes
- > To determine the best pharmaceutical approach to protect vascular health in adolescents with type-1 diabetes in two large trials of (i) metformin and (ii) ACE inhibitors and statins alone or in combination



Professor Caroline Crowther and Ms Philippa Middleton

Health of Women and Babies

Improving the health of women and babies in pregnancy and at birth

To ensure the best health and wellbeing possible for women and their babies, Caroline and Philippa lead high quality and timely maternal and perinatal research. The group runs diverse research programs to encompass the spectrum from preconception through pregnancy and childbirth, infancy and later life. In 2013 the Health of Women and Babies Group continued to advance ongoing major trials which evaluate care during pregnancy and childbirth, for gestational diabetes and treatment of preterm birth. These trials include:

- > **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
- > **IDEAL** - Investigation of dietary advice and lifestyle for women and borderline gestational diabetes
- > **MAGENTA** - Magnesium Sulphate at 30 to 40 weeks Gestational age: Neuroprotection Trial
- > **DIAMIND** - Postpartum reminders to test for type-2 diabetes in women who have experienced gestational diabetes mellitus
- > **PROGRESS** - Progesterone after previous preterm birth for the prevention of neonatal respiratory distress syndrome
- > **BAC** - Birth After Caesarean: Planned vaginal birth or planned elective repeat caesarean for women at term with a single previous caesarean section

Two international individual participant data (IPD) meta-analysis collaborations on treatments prior to preterm birth are nearing completion. These are the AMICABLE (Antenatal Magnesium IPD International Collaboration: Assessing the Benefits for Babies using the Best Level of Evidence) and PRECISE (Prenatal REpeat Corticosteroid International IPD Study Group) studies.

Philippa is collaborating with other Robinson Research Institute members in her role as leader of the research priority Born Too Soon. This interdisciplinary team is working on a number of innovative research proposals to unravel the mechanisms on preterm birth and ultimately find therapies for prevention.

2013 saw the launch of My Baby Movements, which is a new NHMRC cluster trial for preventing stillbirth. Vicki Flenady at the Mater Medical Research Institute, with both Philippa and Caroline as Chief Investigators, is leading the study.

The group also received further funding from the Cerebral Palsy Alliance for the WISH Follow-up Project (Working to Improve Survival and Health for babies born very preterm).

The group revamped their database of randomised trials with help from the Perinatal Society of Australia and New Zealand. The database is proving to be a powerful tool with entries for 400 active or recently active trials, as well as over 100 trials that are currently recruiting or about to recruit.

Philippa and Caroline have a strong focus on Aboriginal health and are undertaking an evaluation of the SA Aboriginal Family Birthing Program. As part of this project over one hundred interviews were conducted with individuals in 2013 – findings will be presented in the first half of 2014.

2013 was also the 20th Anniversary for the Cochrane Collaboration. Caroline, Philippa and colleagues play a major role in the Cochrane Pregnancy and Childbirth satellite, which supports over 200 Australian and New Zealand review authors who contribute to a third of Cochrane and Pregnancy Childbirth reviews published in the Cochrane Library. In 2013 the satellite received UK National Institute for Health Research (NIHR) funding to complete a priority review on 'Asthma and Pregnancy'.

Further to extensive work in trials and reviews, the group continues to be very active in teams developing clinical practice guidelines, including NHMRC antenatal care, Australian and New Zealand guidelines on antenatal corticosteroids prior to preterm birth and New Zealand guidelines on gestational diabetes. Caroline and Philippa were also successful in a bid for a further appointment to the NHMRC Evidence Panel (panel of 'Providers with expertise relevant to the development and presentation of health advice') ensuring a strong translation element to the research work.



Group members

Research fellows: Emily Bain and Tanya Bubner

Research coordinators: Pat Ashwood, Daniela Gagliardi, Michaela Jarrett, Ellen Lyrtzis and Sophie Trenowden

Research support: Carol Holst, Kaye Robinson, Claire Binnion, Melissa Ewens, Mary Paleologos and Elen Shute

Statisticians: Tran son Thach and Lisa Yelland

Data managers: Vincent Ball and Sasha Zhang

PhD and Honours candidates: Angela Brown, Allan Cyna, Shanshan Han, Emer Heatley, Zohra Lassi, Laura Spencer and Zhixian Sui



Professor Michael Davies and Professor Vivienne Moore

Life Course and Intergenerational Health

Understanding how inequalities in the health of women and children arise, through integrated social and biological pathways, and identifying opportunities for change



Group members

Research fellow: Dr Alice Rumbold

Senior postdoctoral researchers:
Dr Wendy March, Dr Melissa Whitrow
and Dr Tanya Zivkovic

Research and teaching academics:
A/Prof Megan Warin and Dr Lynne Giles

Postdoctoral researcher:
Dr Stephanie Champion and Dr
Malinda Steenkamp

Statisticians: Chris Davies, Suzanne
Edwards and Kristyn Willson

PhD candidates: Renae Fernandez
and Renae Kirkham

Research co-ordinator: Kendall Smith

Collaborators: Prof Siladitya
Bhattachary, Dr Dimitry Kissin, Prof
David Phillips and Prof Bianca de
Stavolai

Early life is the foundation for later health and life potential. Growth and development of the child, both before birth and subsequently, are intimately linked to the health and wellbeing of the mother. That, in turn, reflects the mother's current environment, including family relations and socio-economic circumstances, as well as her own intergenerational history.

The Life Course and Intergenerational Health Group seeks to better understand the interplay of social and biological factors that influence health throughout life. The group is especially interested in how chronic diseases and their risk factors are transmitted from parents to the next generation, as well as ways in which this could be addressed to improve health. Within the group, epidemiological research is undertaken with a focus on the developmental origins of congenital malformations, reproductive disorders, type-2 diabetes and cardiovascular disease. Other members undertake anthropological and narrative research in order to understand the social determinants of health and the complexity of significant public health problems (e.g. obesity). The group also considers the political and gender implications of their research findings.

In 2013 the group received international attention for research that showed that the more time women spent in casual employment, the more likely they were to be childless at age 35, irrespective of their socio-economic status. This finding is important as it challenges the pervasive media representations of delayed childbearing as a phenomenon arising from highly educated women postponing motherhood to pursue their careers.

“ In 2013 the group received international attention for research that showed that the more time women spent in casual employment, the more likely they were to be childless at age 35...”

In a separate line of research, the group also reported detailed comparisons of perinatal outcomes for different forms of assisted reproductive technology, indicating which treatment approaches are more conducive to healthy babies. They continued their investigations of child growth, demonstrating that rapid growth before 3.5 years has implications for later obesity and body composition. This is amplified by the presence of a stressor - such as multiple house moves - in early life. The group published evidence that birth weight and the child's subsequent growth path influences insulin resistance in children.

In 2014, the group hopes to contribute new evidence that will lead to improvements in assisted reproductive technology, with a focus on optimising the health of the baby. In relation to growth paths of children, the group is now identifying the underlying environmental or antenatal determinants. They will also continue to advance 'bio-cultural' theory and explore the class and gender dimensions of obesity.

Professor Jodie Dodd

Health of Pregnant Mothers and Babies

Evaluating health care interventions during pregnancy to improve outcomes for mothers and babies

To ensure health outcomes continue to improve for pregnant mothers and their babies, Jodie Dodd leads diverse research programs that challenge maternal fetal care interventions.

Maternal Fetal Medicine

Maternal fetal medicine specialists provide expert diagnosis and ongoing care for women with significant complications during pregnancy, which can put the woman or her unborn baby at risk. Many of these conditions are rare and to investigate efficacy of care requires extensive collaboration with specialists both nationally and internationally.

Fetal anaemia caused by red cell incompatibility is quite uncommon, and is estimated to occur in approximately 0.1-0.6% of all pregnancies. Jodie's group is currently evaluating whether ultrasound assessment of fetal cerebral blood flow velocity can be used to accurately time second and subsequent transfusions for women with red cell alloimmunisation, where the unborn baby is at risk of developing anaemia in-utero.

Multiple Pregnancies

Multiple pregnancies increase the occurrence of health complications in both mothers and infants. Women with a twin pregnancy are more likely to give birth preterm, with approximately 46% able to maintain pregnancy and give birth after 37 weeks of gestation. For women whose twin pregnancy continues beyond this point, risks of perinatal mortality and morbidity increase with advancing gestational age.

In collaboration with a Canadian-led multi-centred randomised control trial the group is comparing vaginal birth with caesarean birth for uncomplicated twin pregnancies. Findings showed in twin pregnancy between 32 weeks 0 days and 38 weeks 6 days of gestation, with the first twin in the cephalic presentation, planned caesarean delivery did not significantly decrease or increase the risk of fetal or neonatal death or serious neonatal morbidity, as compared with planned vaginal delivery.

Obesity during Pregnancy

The number of people who are overweight [Body Mass Index (BMI) 25.0-29.9kg/m²] and obese [BMI >30.0kg/m²] is rising globally, affecting in excess of 110 million children and 1.3 billion adults across the globe. Almost 50% of pregnant women in western societies are entering pregnancy with a BMI above 25kg/m².

High maternal BMI during pregnancy is associated with a greatly increased risk of developing diabetes and cardiovascular disease in women. For the infant, high maternal BMI is a significant predictor of future child and adult obesity.

The group is evaluating the effect of health care interventions during pregnancy on maternal, infant and early childhood health outcomes, including subsequent risk of obesity. Interventions to improve the health of women and their babies include nutrition, physical activity and pharmacological.

During 2013, the group completed recruitment of more than 2,200 women who participated in the randomised LIMIT Trial, evaluating the effect of dietary and exercise advice during pregnancy on maternal and infant health outcomes. This cohort of women and their infants – who are now three years of age – are followed, monitoring growth, development and wellbeing. Work has commenced on the extensive bio-bank collected in this study.

In 2014 Jodie's group will:

- > Collate and report on the results of the study fetal anaemia study
- > Report on the follow up of their multi-centred trial of elective birth at 37 weeks versus expectant management
- > Recruit 1,300 women to a randomised trial of an insulin sensitising drug called metformin to restrict weight gain in overweight and obese pregnant women
- > Study the impact of healthy diet and physical activity advice in women with a normal BMI by recruiting more than 1,500 women to an intervention of lifestyle advice or routine care
- > Continue metabolic, genetic and metabolomic analyses of the LIMIT Trial Bio-bank.



Group members

Research manager: Andrea Deussen

Research fellows: Rosalie Grivell and Lisa Moran

Principal scientist: Julie Owens

Clinical researchers: Andy McPhee, Chad Anderson and Ross Haslam

Research coordinators: Courtney Cramp and Angela Newman

Statisticians: Lisa Yelland and Thach Tran

Laboratory coordinator: Anne MacPherson

PhD candidate: Tulika Sundernathan

Research assistants: Ashlee Fairclough, Caroline Holst, Louise Fraser Lavern Kannieappan, Anita Lo, Danielle Post, Caroline Sheppard, Gozia Smezja, Heather Webb, Kate Welldon, Sui Zhixian and Stephanie Zrim

Research midwife: Meredith Kelsey

Research support: Greg Beaumont, Caroline Holst and Jacqueline Smith

Data management: Vincent Ball and Sasha Zhang

Emeritus member: Jeffrey Robinson

Collaborators: Matthew Gillman, Debbie Lawlor and Lucilla Poston



Professor Antonio Ferrante

Developmental and Genetic Immunology

Understanding the molecular and cellular basis of chronic disease development and treatment in childhood

Group members

Principal scientist: Charles Hii

Senior scientists: Nick Gorgani, Hameet Singh and Neal Trout

Scientists: Yefang Ma, Bernadette Boog, Sarah Harvey, Yonggin Li, Nick Mabbarrack, Clare Mee and Alex Quach

PhD candidates: Usma Munawara and Cheung Szevan

MSc: Yun Lao

Pathologist: Tatjana Banovic

Student: Thanh Lam

Key collaborators: Suresh Mahalingam, Catherine Abbott, Susan Prescott, Paul Anderson, Howard Morris, Pravin Hissaria, Patrick Quinn, Mike Gold, Jenny Couper, Declan Kennedy, Sharon Choo, and Anthony Smith

Chronic inflammatory conditions such as arthritis, diabetes and inflammatory bowel disease, are a major cause of disability and chronic pain, and pose a significant economic burden to the community. There is even greater concern when diseases begin in early childhood. Despite research advancements over the last two decades in the treatment and management of patients with inflammatory diseases, the lack of an appropriate understanding of the cellular and molecular networks operating in disease establishment and resolution limits significant improvements in clinical practice.

The Developmental and Genetic Immunology Group is working on identification of cell subpopulations, inflammatory mediators and intracellular messages, which form the signaling axis(s) that induces and promotes the development of these inflammatory diseases. The group will develop both a drug and nutrient supplement approach and each will be explored for treating patients with these conditions.

This group has identified a new control point in the inflammatory response that is relevant to several diseases including type-1 diabetes, inflammatory bowel disease and rheumatoid arthritis/juvenile idiopathic arthritis. This control point is the expression of the Complement Receptor Immunoglobulin (CRIg). This receptor is exclusively expressed on macrophages, a cell which plays a major role in tissue damage associated with these diseases. While CRIg is primarily known for mediating protection against infection it also has anti-inflammatory and immunosuppressive properties. Current evidence associates increased expression



of this receptor with low inflammation. This group observed cytokine networks promoting or protecting against inflammatory diseases control the expression of this receptor. Tony's group has now developed a nutritional approach to control this expression using vitamin D.

The group is doing further studies into the intracellular signalling pathways, which control the expression of CRIg on macrophages. This includes the role of protein kinase C that may be the central regulator of CRIg expression. The link between vitamin D and CRIg in inflammatory conditions will be further examined.

Professor Jozef Gecz

Neurogenetics

Investigating the genetics and biology of human neurological disorders

Neurological disorders are diseases of the nervous system which result in disabilities or functional limitations. In childhood, neurological disorders are common – with intellectual disability, epilepsy and cerebral palsy affecting up to 3-4% of children. The genetics of these brain disorders are extremely complex. To date we know of at least 600 intellectual disability genes and 300 epilepsy genes. A handful of cerebral palsy genes have also been identified and there are likely many more. Finding the causative gene and the genetic mutation responsible for these disorders is therefore a major challenge.

The Neurogenetics Group aims to understand the neurobiology of human brain function by studying major neurological disorders which are genetically determined. By identifying and characterising the mutations implicated in intellectual disability, epilepsy and cerebral palsy, a greater understanding of the role of specific genes and proteins in normal brain function can be discovered.

In 2013 Jozef's group discovered, or made major contributions to, the discovery of several novel genes causing epilepsy (DEPDC5), intellectual disability (USP9X and ZC4H2) and cerebral palsy (NKX2.1 and ZC4H2). Jozef and colleagues also revealed the crucial role for the non-sense mediated mRNA decay (NMD) pathway in neuronal cell (in particular neuronal stem cell) function, as well as implicating five other NMD genes in neurodevelopmental disorders. These genes include UPF2, UPF3A, SMG6, EIF4A3 and RNPS1.

Significant progress was also made to better understand disorders through genes identified in previous years, including GOSR2 for myoclonic epilepsy (North Sea Epilepsy), TBC1D24 for intellectual disability and epilepsy, as well as CCDC22 and ARX for intellectual disability.

In 2014 Jozef will continue to focus on finding genetic determinants of neurological disorders in childhood with specific attention to cerebral palsy, female limited epilepsy and intellectual disability.



Group members

Senior scientist: Mark Corbett

Research officers: Lachlan Jolly, Duyen Pham, Raman Sharma and Clare van Eyk

Research assistants: Rasha Alhamra, Renee Carroll, Alison Gardner, Marie Shaw and Joshua Woenig

PhD candidates: Claire Homan, Gai McMichael, Lam Son Nguyen and Stanley Tan



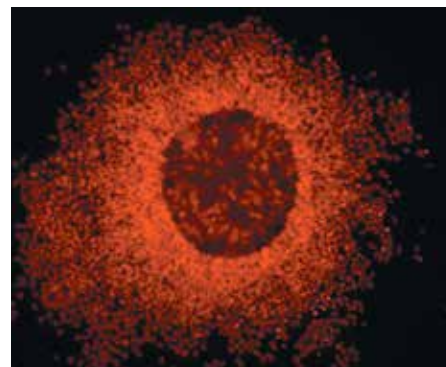
Associate Professor Robert Gilchrist and Dr David Mottershead

Oocyte Biology and Growth Factor Laboratories

Investigating ovarian folliculogenesis, oocyte maturation and embryo development, to provide new therapies for infertile couples

Oocytes are rate limiting for female fertility and oocyte quality is difficult to define and measure. Understanding the molecular mechanisms underpinning oocyte-somatic cell communication is important for the development of new infertility treatments and for new reproductive technologies.

In 2013, the Oocyte Biology and Growth Factor Laboratories Group produced several papers on the role of epidermal growth factors-like peptides and their roles in oocyte maturation, including their interactions with cAMP-activated signalling during oocyte maturation. The oocyte-secreted growth factors, GDF9 and BMP15 biology, continued to be a focus, particularly determining which forms and doses of proteins can improve oocyte quality and developmental potential during IVF.



At the conclusion of 2013, Robert Gilchrist and David Mottershead have both taken new career opportunities outside the University of Adelaide. Rob now heads a research unit at The University of New South Wales in Sydney but remains an Affiliate Associate Professor with the University of Adelaide. David is at the Julius-von-Sachs Institute of the University Würzburg, Germany. Rob and David remain active collaborators with the Robinson Research Institute.

Group members

Research officer: Lesley Ritter

Research assistants: Xiaoqian Wang and Melissa White

Cook Medical Adelaide Visiting Research Fellow: Xiaoying Zheng

Visiting scientists: Li Haijun, Satoshi Sugimura, Haitao Zeng and Li Jingjie

HDR candidates: Dulama Richani, Ryan Rose, Jacqueline Sudiman and Georgia Martin

Collaborators: Michel De Vos, Craig Harrison, Ken McNatty, Thomas Muller, David Robertson, Johan Smitz, Peter Stanton, Jose Buratini, Joy McIntosh

Associate Professor Michael Gold

Allergy and Vaccine Safety

To ensure health outcomes continue to improve across generations, Michael Gold leads two research programs in the areas of allergy and vaccine safety

Preventing and management of food allergy and allergic disease

In western and developed countries there has been an evolving epidemic of allergic disease. An increasing number of children under five years of age are developing food allergies. Recent studies have shown that one in ten Australian children aged 12 months have an egg allergy, the highest documented rate in the world. The Allergy Group's goal is to understand the immunological mechanisms associated with the prevention and management of egg allergy and in particular to understand the role of egg exposure in the development of tolerance to egg. Preventing and treating egg allergy has the potential to provide significant public health benefits.

In 2013 recruitment continued for the STEP trial (Starting Time for Egg Protein) a RCT of early versus late introduction of egg into an infants diet. This study once completed will provide evidence based feeding guidelines for Australian infants. A PhD student (Merryn Netting) commenced the CAKE (Can Egg Allergic Kids Eat Egg) study, an RCT investigating the possible therapeutic benefit of heat-treated egg in inducing egg tolerance in allergic children. Follow ups continue with a cohort of children (now aged six years) whose mothers participated in an RCT of fish oil supplementation in pregnancy. This is the basis of a further PhD (Karen Best) student's work. Initial results have demonstrated a possible protective effect for egg sensitisation. Since this is a risk factor for the development of asthma, the follow up of this outcome is critical.

In 2014 the CAKE studies will be completed and data analysis will occur which will ascertain the effectiveness of exposure to heat-treated egg in the treatment of egg allergy.

Developing new ways to monitor the safety of vaccines

When a new or seasonal influenza vaccine is licensed for use, safety information about potential rare reactions is incomplete. The current system of surveillance for these events lacks the capability to detect these reactions in a timely way. The Vaccine

Safety Group aims to address the current deficiencies in surveillance by exploring health provider reporting, active sentinel surveillance and e-Health, including data linkage. This is of critical importance due to increasing public concern about vaccine safety.

The group seeks to understand how adverse events following immunisation are reported by parents and health providers, and to develop strategies to enhance reporting. In addition, research is focused on using e-Health for detecting and analysis of a vaccine safety signal, and in investigating individual children who have experienced adverse vaccine reactions.

In 2013 significant barriers to data access were overcome for the VALiD (Vaccine Assessment using Linked Data), which is an ARC funded study, in terms of data transfer to the Australian Institute of Health and Welfare for data linkage. The study will link the Australian Childhood Immunisation Register with the national death Index and state based morbidity data from multiple jurisdictions. This project is unique and regarded as ground-breaking by linking Commonwealth and State data. VALiD is the subject of a current PhD project (Katherine Duszynski). In 2013, PhD degrees were awarded to candidates Jesia Berry and Vicki Xafis. A further PhD candidate (Adrianna Parrella) successfully submitted her thesis, which examined parental and provider reporting of adverse events following immunisation.

In 2013 the group were successful in obtaining an NHMRC project grant for the STARSS (Stimulated Telephone Assisted Rapid Safety Surveillance) study. This randomised controlled trial will investigate a novel method for safety surveillance using e-Health for surveillance. Additionally, the group has been involved in collaborations with national researchers and networks in the area of vaccine safety; firstly, through sentinel surveillance – the Paediatric Adverse Event and Disease Surveillance (PAEDS) network, which includes four tertiary care hospitals in surveillance activities - and secondly, with an NHMRC funded study, to examine convulsions after vaccination.



Group members

Chief investigators: Annette Braaunack-Mayer, Patrick Quinn, Maria Makrides, Imme Penttila, Declan Kennedy and James Martin

Chief investigator and biostatistician: Phil Ryan

Chief investigator: Helen Marshall

Statistician: Peter Baghurst

Bioethicist: Annette Braaunack-Mayer

Project manager: Gabriella Lincoln

PhD Candidates: Jesia Berry, Katherin Duszynski and Adriana Parrella

Research nurses: Christine Heath, Mary Walker, Merryn Netting and Karen Best



Group members

Research fellow: Agnes Arthur

Postdoctoral researchers: Dimitrios Cakouros and Esther Camp-Dotlic

Research assistant:
Romana Panagopoulos

Technical officer: Sharon Paton

PhD candidates: Lachlan Cooper,
Sarah Hemming and Thao Nguyen

Honours student: Yi Yan Janice Lim

Professor Stan Gronthos

Mesenchymal Stem Cells

Origins and biological properties of mesenchymal stem cell populations

Adult bone marrow is thought to contain a population of self-replicating multi-potential stem cells referred to as mesenchymal stem cells. Mesenchymal stem cells have potential as novel therapeutic agents for repairing damaged connective tissue due to trauma, disease or congenital conditions. The Mesenchymal Stem Cell Group, in collaboration with Professor Andrew Zannettino, has developed novel stem cell isolation technology to identify mesenchymal stem cell-like cells from adipose tissue and dental tissues that exhibit similar growth properties and gene expression profiles to those identified in bone marrow. This work has resulted in the generation of several patents encompassing the isolation and expansion technologies and use of different mesenchymal stem cell preparations for various tissue engineering based applications. These patents have now been licensed to two sister companies: Angioblast Inc. (New York, New York) and Mesoblast Ltd. (Melbourne, Victoria).

The Mesenchymal Stem Cell Group is now the leading group worldwide with the technology to purify mesenchymal stem cells directly from human tissue using its own patented isolation protocols. Work conducted during 2013 addressed:

- > Identification of factors that regulate bone fracture healing
- > Demonstration that specific epigenetic changes in mesenchymal stem cells control cellular senescence and life span

- > Identification of the mechanisms of mesenchymal cell development from inducible pluripotent stem cells
- > Pre-clinical studies demonstrating efficacy of mesenchymal stem therapy in ischaemic stroke, cardiac disease, intervertebral disk degeneration and periodontal disease
- > Identification of factors central to mesenchymal stem cell-mediated regulation of haematopoiesis, angiogenesis and immune cell modulation, with potential implications in understanding tumour cell development

Together with commercial partner Mesoblast Ltd., the Mesenchymal Stem Cell Group is moving forward into Phase II/III human clinical trials for orthopaedic and cardiovascular applications using mesenchymal stem cells. Furthermore, Phase II/III human trials are being conducted to assess the efficacy of ex vivo expanded cord blood on mesenchymal stem cell feeder layers for the reconstitution of bone marrow in cancer patients following ablative therapy. Continuing research into the basic properties of mesenchymal stem cells will help develop effective and safe therapeutic strategies in the future for a wide variety of clinical indications.

Associate Professor Frank Grutzner

Mammalian Reproduction Group

Comparing genetic and epigenetic mechanisms in different mammalian species, to understand how genetic and epigenetic mechanisms contribute to human diseases such as infertility, cancer and diabetes

The comparison of genes, genomes and epigenetic mechanisms in different species has provided fundamental insights into how genes function in humans, how certain changes evolved, and how this contributes to disease. Studying genes in species distantly related to humans sheds light on metabolism and cancer, and has helped the development of novel drugs for diseases including type-2 diabetes.

The Mammalian Reproduction Group studies gene evolution in mammalian species distantly related to humans – monotremes in particular. Monotremes (platypus and echidna) have an extraordinary sex chromosome system that can reveal novel genes and pathways involved in sex determination and differentiation in all mammals, including humans. Monotremes have undergone radical changes to their stomach anatomy and physiology. This is accompanied by a massive loss or change of genes involved in digestion. By studying

monotremes, we have the opportunity to identify the role of key genes involved in stomach function and metabolism in humans and other mammals. Such research may lead to the identification of new therapeutic targets for metabolic diseases such as diabetes.

In 2013 the group continued to investigate the role of genes in the piRNA pathway in ovary and ovarian cancer. They also embarked on new work to investigate if the interaction of genes in the nucleus has changed in ovarian cancer when compared to normal cells. Researchers discovered a gene that is important in metabolic control in humans and other mammals, is missing in the platypus while its receptor is still present. This suggests that other molecules must be acting on this receptor and these genes may also be able to activate the same receptor in other mammals and humans.

In 2014 the group will increase their research into the function of non-protein coding RNAs pathways and long-range gene interactions and their role in ovarian cancer and sex chromosome biology. Frank's group will also further compare genes involved in metabolic control in humans and platypus with the aim to better understand the genes involved in insulin release. This research may lead to new treatment options for type-2 diabetes.



Group members

Lecturer: Tasman Daish

Visiting Research Fellow:

Dan Kortschak

PhD candidates: Aaron Casey, Chuan He, Reuben Jacob, David Stevens, Deborah Toldo-Flores, Nicole Williams and Megan Wright

Collaborators: Peter Donnelly, Briony Forbes, Henrik Kaessman and James Turner

“...such research may lead to the identification of new therapeutic targets.”



Group members

Clinical researcher: Suzette Coat

Consultant: Rachel Hughes

PhD candidate: Mansi Dass Singh

Professor Bill Hague

Obstetric Medicine Research

Improving outcomes for pregnant women with medical complications

Pregnancy is affected by medical complications in over 10% of all women. Some complications may predate the pregnancy while others develop during or after pregnancy. In certain cases, complications may threaten the lives of both mother and baby. Early identification and appropriate therapy is vital; however, the research base for therapeutic decisions can be limited with minimal good evidence to support it.

The predominant focuses of the Obstetric Medicine Research Group are the two major medical disorders of pregnancy: gestational diabetes and pre-eclampsia. The group are the lead site for the Australian follow-up of two major studies. The first is the MiG trial, assessing the offspring of women with gestational diabetes who were treated with either metformin or insulin. The second is the Folic Acid Clinical Trial (FACT), an international study to examine whether folic acid taken in the second and third trimesters

can help to prevent pre-eclampsia, with particular interest in how the impact of folic acid on one carbon metabolism might affect DNA damage as well as maternal and fetal epigenetics in women with pre-eclampsia.

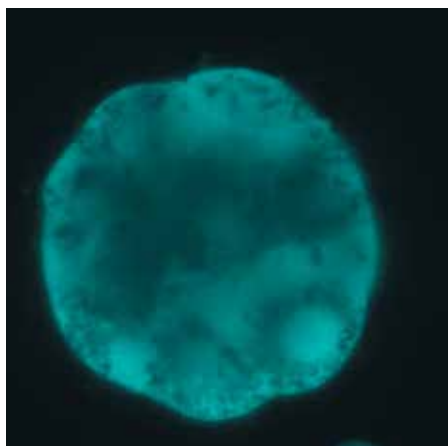
The group has completed the follow-up of the six to seven year old offspring of the MiG study in Adelaide. No impact of fetal exposure to metformin on cognitive or motor skill development has been demonstrated. This is an ongoing study and the group are continuing to follow up the Adelaide cohort.

The group have initiated the FACT study in four more Australian centres, with ongoing and increasing recruitment across Australia as well as in Adelaide. They have also designed a national randomised trial of the proposed new national guidelines for the diagnosis and management of women with gestational diabetes.

Associate Professor Leonie Heilbronn

Metabolism and Health

Assessing the metabolic consequences of ovarian stimulation and in vitro fertilisation



The number of children and adults conceived by in vitro fertilisation (IVF) now totals more than five million across the world. Accumulating evidence suggests that IVF children have altered health profiles as compared to their non-IVF peers, including increased body fat, raised blood pressure, increased fasting blood glucose and triglycerides and lower flow mediated blood vessel dilation. Adult mice conceived by IVF also show increased body fat and fasting insulin, increased systolic blood pressure, and impaired glucose tolerance.

The Metabolism and Health Group aims to provide new insights regarding long-term health consequences of IVF, and drive further research into best practice. The group recently showed that adult humans conceived by IVF displayed significantly lower insulin sensitivity by clamp, as compared to age and body mass index matched control adults conceived naturally. Such changes may be associated with

increased risk of type-2 diabetes later in life. However, human studies cannot determine whether these differences are due to the IVF procedure itself or are a result of genetics, socio-economic status, or parenting differences between these groups.

To help understand the medical influences in this equation, Leonie directed research efforts on mouse studies. These studies aimed to determine if metabolic changes are associated with the process of controlled ovarian hyperstimulation used to collect eggs for IVF, and/or in vitro culture of embryos.

Leonie and colleagues observed gender specific consequences of fertility treatments in mouse offspring. Male mice conceived by IVF displayed impaired glucose tolerance and insulin resistance in the liver when they were both lean and obese. Male mice conceived following ovarian stimulation (OS) only did not display these conditions, as compared to naturally conceived animals, suggesting that it is the process of IVF itself that may increase the risk of type 2-diabetes. This is in contrast to the results observed in females, whereby female IVF and OS mice consuming regular chow diet displayed no impaired glucose tolerance or insulin resistance). However, both groups of females were more susceptible to the metabolic consequences of obesity, and were at increased risk of developing type-2 diabetes. This suggests that ovarian stimulation alone may program metabolic consequences later in life but that obesity conditions are required to unmask these effects.

Leonie is currently focussing on confirming and extending these results to establish why differences in metabolic risk factors are observed.



Group members

Postdoctoral researcher: Amy Ryan

PhD candidates: Thomas Butler, Miaoxin Chen and Bo Liu

Research assistant: Briohny Bartlett



Professor Stefan Hiendleder

Epigenetics and Genetics

Understanding epigenetic and other non-mendelian genetic mechanisms and programming in prenatal development to optimise birth weight and pregnancy outcomes

Birth weight is strongly associated with developmental capacity and the achievement of positive health outcomes throughout life. It is now clear that weight at birth is determined not only by genes that are inherited in a classical mendelian genetic fashion, but also by epigenetic mechanisms such as imprinting, which regulate gene expression and phenotype at a higher level above the primary DNA code. Work performed by the Epigenetics and Genetics Group and others, demonstrates that interactions between classical mendelian genetic, non-mendelian genetic and epigenetic mechanisms, and factors shape prenatal development and phenotype at birth in a sex-specific manner.

Stefan's group focuses on dissection of the complex molecular genetic architecture of birth weight. They identify novel epigenetic and genetic effects on birth weight and their interactions with environmental factors. This allows the group to identify risk factors and to develop intervention strategies for optimal outcomes at birth.

The group used an animal model to determine effects of parental genomes, fetal sex, and non-genetic maternal factors on fetal skeletal muscle and bone at midgestation. They identified for the first time specific contributions of the maternal and paternal genome to muscle fibre characteristics and muscle mass as well as bone parameters and their serum correlates. Furthermore, they demonstrated that abundance of the imprinted maternally expressed miRNA harbouring long non-coding RNA H19 is correlated with skeletal muscle and bone phenotype. The group and others have previously shown plasticity of H19 expression in human conception and present data suggests H19 is an epigenetic sensor.

Current work focuses on detailed molecular dissection of maternal and paternal epigenetic genetic effects on fetal and placental phenotype.



Group members

Research manager: Dana Thomsen

PhD candidates: Consuelo Estrella, Mani Ghanipoor-Samami, Ali Javadmanesh, Entesar Shuaib and Ruidong Xiang

Key collaborators: Brian Burns, Kathy Gatford, Karen Kind, Sergio Ledda, Julie Owens, Mark Nottle, Claire Roberts, Susanne Ulbrich and Cory Xiang

Dr Louise Hull

Endometriosis

Developing diagnostic and therapeutic tools to help women with Endometriosis

Endometriosis is a painful condition that impacts the lives of about 10 per cent of women. Surgery is required for diagnosis and medical therapies ameliorate symptoms rather than inhibit the disease. There is a need for better diagnostics and therapeutics for endometriosis which the Endometriosis Group is addressing using mouse models and microRNA technology.

Louise's group are determining if plasma microRNAs have diagnostic potential in endometriosis. The group is also exploring ways of manipulating the macrophage response of women to inhibit disease progression using knockout mouse models of endometriosis.

In 2013 the group identified plasma microRNAs with diagnostic potential. They also found that altered macrophage activity could suppress lesion development in models of endometriosis. They hypothesise that microRNA regulation of macrophages could alter disease outcomes for women with endometriosis.

Going forward, Louise seeks to confirm the diagnostic findings in a large cohort of patients. The group is also looking at microRNA manipulation in mouse models to alter endometriosis disease progression.



Group members

Senior postdoctoral scientist: Jonathan McGuane

Postdoctoral scientist: Zhao Wang

PhD candidates: Zahied Johan and Vicki Nisenblat

Honours student: Katherine Watson

Summer student: Gabriel Kuo



Associate Professor Wendy Ingman

Breast Biology and Cancer

Investigating mammary gland biology in health and disease

Group members

Postdoctoral researchers:

Pallave Dasari and Danielle Glynn

Research officer: Leigh Hodson**Research nurse:** Kathryn Mildren**PhD candidates:** Siti Noordin and Sally Sun**Master student:** Vahid Atashgaran**Honours student:** Maddison Archer and Harshani Pedige**Summer student:** Vivian Lee

Collaborators: Kara Britt, Andreas Evdokiou, Louise Hull, Mark Hutchinson, David Kennaway, Marina Kochetkova, Malcolm Pike, Fiona Pixley, Sarah Robertson, Rik Thompson and Wayne Tilley



The breast is one of the most prominent secondary sexual characteristics in women, and yet scientists still understand little about how this tissue functions in health and disease. Breast cancer is the most prevalent cancer type among women, with over 13,000 new cases diagnosed each year in Australia and the incidence of this deadly disease is rising. Another breast disease, mastitis, is a common and poorly understood inflammatory condition that plagues women during lactation, causing pain, fever, low milk supply and early cessation of breastfeeding.

The Breast Biology and Cancer Group aim to:

- > Understand why the breast has such high susceptibility to cancer and the biological mechanisms that increase women's risk of developing the disease
- > Work towards developing novel therapies that reduce breast cancer risk
- > Examine the cellular mechanisms that lead to breast inflammation in mastitis
- > Investigate potential therapies to quickly and effectively prevent the symptoms of mastitis

A major focus for Wendy and colleagues in 2013 was expanding previous research on the role of macrophages in menstrual cycle-associated breast cancer risk. Immune

cells called macrophages usually help to protect our bodies from cancer, but Wendy discovered that the fluctuating levels of hormones that women experience each month actually affects how these cells function in breast tissue. The research suggests that there is a window of risk that opens up each month around the time a woman has her period, when immune defences are down, and the breast could be more susceptible to the initiating factors that can lead to cancer. In 2013 Wendy also made exciting progress towards developing a novel therapy for mastitis. The group demonstrated that low milk supply associated with mastitis is actually the result of TLR4-mediated inflammation, rather than the infection itself. Steps towards translation of this research were also taken with a provisional patent filed in July.

Wendy is now working to extend findings on the relationship between immune cells and breast cancer risk through analysis of how hormones affect human breast tissue – the group is taking some exciting steps towards dissecting the cellular and molecular mechanisms involved in this phenomenon. Wendy is also seeking to progress initial successes in understanding TLR4 in mastitis into clinical applications.

Professor David Kennaway

Circadian Physiology

Investigating the impact of disruption of circadian rhythms on physiological processes

More than 1.4 million Australians work outside normal working hours. Shift work and increased light exposure at night has been associated with poor sleep and fatigue, resulting in workplace accidents and incidents. But now, there is emerging evidence that shift work is a significant public health issue - with workers being at significantly higher risk of developing or exacerbating chronic diseases. These include an increased risk of Metabolic Syndrome, in particular vascular events, diabetes or impaired glucose tolerance, elevated BMI and obesity, as well as adverse impacts on fertility and pregnancy.

Currently we are unable to define why night-time activity and daytime sleep increase the risk of developing or exacerbating chronic diseases; but one strong possibility is that this lifestyle disrupts fundamental cellular circadian rhythms that are essential for normal physiological functions.

The Circadian Physiology Group is working towards understanding the consequences of shift work on the metabolic health of men and women, the fertility of women and the health of their children. While animal models cannot replicate actual human shift work, a key innovation in David's research is the approach of simulating the circadian rhythm disruption of human shift work, such as altered light/dark cycles, timed food access, and diet quality, all of which can be tested in humans.

David and colleagues have previously shown that disrupting maternal circadian rhythms - through exposure to chronic phase shifts of

the photoperiod - has lifelong consequences for the metabolic homeostasis of the fetus, such that offspring develop increased adiposity, hyperinsulinaemia and poor glucose and insulin tolerance. During 2013 David conducted experiments to determine the mechanisms by which these poor metabolic outcomes arise. The group found that disruptions of the photoperiod can severely disrupt normal circadian profiles of plasma hormones and metabolites, as well as gene expression in maternal and fetal tissues. Disruptions in the timing of food consumption and the downstream metabolic processes required to utilise that food, may lead to reduced efficiency of growth whereby maternal weight gain is reduced during early embryonic development. It is these perturbations that may contribute to the programming of poor metabolic homeostasis in the offspring.

During 2013 David investigated the utility of a large animal model for studies on circadian rhythm disruption, which would permit the group to address questions not possible with the rodent models. Adult sheep were subjected to four weeks of photoperiod changes aimed at causing rhythm disruption. This showed that this is indeed a viable model, allowing the group to obtain a large amount of physiological information from a small number of animals. In 2014 and beyond David will use rodent and sheep models to gain further insight into the effects of rhythm disruption on fertility, early embryo development and pregnancy outcomes.



Group members

Research fellows: Michael Boden and Tamara Varcoe

Research officers: Leewen Rattanatray, Mark Salkeld and Athena Voultsios

Collaborators: Glenn McConell, Amanda Page and Shantha Rajaratnam



Group members

Co-directors: Kurt Lushington and James Martin

Research leader: Yvonne Pamula

Affiliate members: Mathias Baumert, Anna Kontos, Silvia Pignata, Tony Ferrante, Quenten Schwarz, David Wabnitz and Scott Willoughby

Professor Declan Kennedy

Sleep Disorders

Evaluating vascular function in children with sleep disordered breathing

Upper airway obstruction during sleep affects 4% of children. The Sleep Disorders Group have previously shown that this is associated with neurocognitive deficits and, more recently, that it may be associated with changes in vascular function including blood pressure.

The Sleep Disorders Group aims to evaluate the controlling mechanisms of the putative changes in vascular function in children with upper airway obstruction during sleep. They also aim to evaluate if treatment results in a return to normal vascular parameters.

In 2013 the group focused on the evaluation of vascular responsiveness in normal children compared to those with sleep-disordered breathing. This work is on-going. Collaborations were developed with authorities in the fields of immunology (Professor Ferrante), neurovascular research (Dr Schwarz), otorhinolaryngology (Dr Wabnitz) and endothelial function (Dr Willoughby).

The group have also been exploring the impact of disturbed sleep on brain development. This work has involved the examination of sleep and neurocognition in children with disorders that disrupt sleep including eczema, diabetes and cystic fibrosis.



Professor Simon Koblar

Stroke Research

Investigating the genetic, proteomic and clinical risks for stroke and the outcomes of stem cell therapy

Sixty thousand Australians suffer a stroke every year and one third are left with severe disability. One therapeutic strategy for treating stroke is to transplant adult tissue-derived stem cells that have the ability to differentiate into neurons and replace the function of damaged cells. The Stroke Research Group aims to improve stroke outcomes by administering adult dental pulp stem cells (DPSC). The group has previously demonstrated that DPSC injected into the brain of rats can improve neurological function after stroke. The group also participates in the Australian Stroke Genetics Collaboration, a multi-state, multi-centre Australian study into genetic causes of stroke.

In 2013, the group continued their research into DPSC treatment for stroke, administering DPSC intravenously into stroke-affected mice. They hope that this more clinically relevant method of administration will have a positive effect on brain function. The group also began developing a chronic mouse model of stroke for the assessment of DPSC therapy on long-term disability. The group's investigations into the mechanism of action of DPSC suggest that these adult stem cells may be effective in both the acute and chronic phase of disease. Determining how DPSC improve brain function is of ongoing interest.

In 2013 the group investigated Npas4, a brain-specific transcription factor, and its role in neurogenesis and stroke. Dr Thomas Klaric rejoined the group as a postdoctoral research fellow.

PhD candidate Ms Kylie Ellis finalised her work on neuronal differentiation of DPSC and submitted her PhD in 2013. PhD candidate Mr Michael Djukic is finalising his proteomic biomarker research in transient ischaemic attack (TIA) patients and has discovered further biomarkers with potential Intellectual Property applications. Dr Elaine Leung is finalising her PhD defining characteristics of TIA assessment and management to determine if a community-based rapid access TIA clinic improves patient stroke outcome.

Dr Wai Khay Leong's PhD on the functional use and underlying mechanisms of using DPSC in a rat stroke model was conferred early in 2013. This has led to a successful biotechnology business partnership. A third year medical student, Ms Rebekah Chew, started with the group as a summer scholarship student before undertaking an honours year in 2013, studying the ability of teeth from older adults to produce DPSC and was awarded first-class honours.

Simon's group is part of a multi-institutional research project on neuroplasticity in stroke that has been awarded NHMRC funding worth \$735,660 from 2014 to 2017. Titled 'Characterising post-stroke cortical plasticity in humans – identifying a critical window for rehabilitation', the project will enrol patients from Stroke Units at both the Royal Adelaide Hospital and The Queen Elizabeth Hospital.



Group members

Co-director, SRP:

Anne Hamilton-Bruce

Head, Acute Stroke Unit, The Queen Elizabeth Hospital:

Jim Jannes

Research fellows:

Thomas Klaric, Karlea Kremer and Martin Lewis

PhD candidates:

Fong Chan Choy, Michael Djukic, Kylie Ellis, Joshua Winderlich and Elaine Leung

Summer scholarship students:

Jackie Gowland and Joule Juan Li

Masters candidates:

Wenru Pan and Jenny Sutton

Honours student:

Rebekah Chew

Senior medical scientist:

Austin G. Milton

Research assistant:

Xenia Kaidonis



Group members

Research fellow: Tod Fullston

PhD candidates: Tristan Hardy, Leanne Pacella, Nicole McPherson and Helena Shehadeh

Research assistants: Wan Xian Kang, Lauren Sandeman and Marni Spillane

Honours students: Katherine Ferres, Priya Krishna, Joseph Shirren and Samuel Tilley

Affiliate members: Kathryn Gebhardt and Deirdre Zander-Fox

Dr Michelle Lane

Gamete and Embryo Biology Group

Investigating how environmental exposures to gametes and embryos impact pregnancy and long-term health outcomes

Exposures to environmental factors in both women and men pre-conception, has been shown to influence fetal growth in utero and impact long term health outcomes and susceptibility to metabolic disease. This programming of health is clearly mediated by changes to the gametes – eggs and sperm – which are passed to the embryo at fertilisation. The Gamete and Embryo Biology Group is investigating how the environment impacts gametes, how this is translated to the embryo, and whether it can be reversed. Their research has determined that obesity in males affects the molecular structure of sperm, altering the epigenome of the sperm, which results in offspring with impaired metabolic and reproductive health outcomes.

In 2013, the group determined that male obesity has the ability to be transmitted to two

generations, affecting the metabolic health of the offspring. They also established that male obesity alters the methylation status of germ cells in the testes and that microRNA content of sperm is altered. They found that both diet and exercise interventions in animal models of male obesity prior to conception, improves the fertility of the male and improves the development and health of the subsequent embryo.

Other research focused on new ways to culture mammalian embryos to improve pregnancy and offspring health. They are also researching the role of mitochondria in establishing the molecular signature in ovarian cells.

Michelle's group continues to investigate the underlying mechanism of how parental health cues are transmitted to the next generation with a focus on translating research findings to humans.



Group members

Project officer: Jessica Broadbent

Research officers: Michael O'Callaghan and Clare Van Eyk

Administrative assistants: Corrine Reynolds and Kelly Harper

PhD candidates: Gai McMichael and Joshua Woenig

Affiliates: Christopher Barnett, Mark Corbett, Jozef Gecz, Eric Haan, Raymond Russo and Suzanna Thompson

Collaborators: Evan Eichler, Daniel Geschwind, Richard Gibbs, Eric Hoffman and Andes Moreno de Luca

Emeritus Professor Alastair MacLennan

Cerebral Palsy

Discovery of new inherited and de novo genetic variants causing cerebral palsy

The causes of cerebral palsy, the most common motor neurodevelopmental disorder of childhood, are mostly unknown - inhibiting its prevention. Worldwide the estimated financial cost is \$300 billion but the social cost to the affected children and families is beyond estimate. In Australia there are approximately 34,000 people with cerebral palsy, with incidence 1 in 400 births – that's one child diagnosed every 15 hours.

The Cerebral Palsy Research Group is investigating genetic causes of cerebral palsy using new generation genomic sequencing, and correlating possible environmental (epigenetic) interactions. The ultimate goal is to prevent cerebral palsy by using genetic markers to identify children at risk before they are born so that clinicians can focus on reducing trigger events that may occur during pregnancy.

Alastair and colleagues have established a unique DNA cerebral palsy biobank

with case and parental samples linked to a detailed de-identified clinical databank. This has attracted collaborations from one German and five United States genetic laboratories. Published results have shown that 20% of sporadic cases have potentially pathogenic inherited mutations. In addition, Exome Sequencing studies awaiting publication have shown exciting and novel data about de novo (non-inherited) mutations in these cases. Alastair's group has also described new mutations in families with more than one member with cerebral palsy. In 2013 Alastair and colleague Dr Michael O'Callaghan also published results which proved that caesarean births do not prevent children from developing cerebral palsy. The study showed that while caesarean rates have increased more than six-fold over the last 40 years in Australia, the incidence of cerebral palsy has remained at 2-2.5 per 1000 births.

Associate Professor Helen Marshall

Vaccines and Immunisation Group

Improving effectiveness of vaccine programs for children, pregnant women and adolescents to reduce death and disability from serious infections



The Vaccines and Immunisation Group is focused on improving protection against serious infectious diseases that cause death and disability in infants, children and adolescents particularly including influenza, whooping cough and meningococcal disease. Previous research has been directed towards public health infectious disease priorities such as the H1N1 influenza pandemic and the recent pertussis epidemic with direct translation of research outcomes to child health and public health policy. Influenza remains a serious threat with increased morbidity and mortality for pregnant women as evidenced during the 2009 influenza pandemic. Whooping cough causes deaths in young infants, particularly those too young to be immunised. Invasive meningococcal disease (IMD) causes death and severe disability in children and adolescents despite availability of effective vaccines against some meningococcal strains. This group evaluates the safety and effectiveness of new vaccines designed to prevent serious infections, to ensure vaccines are safe and effective before they are introduced into immunisation programs. They then assess the effectiveness of these vaccines once they are introduced into

the community to ensure vaccines provide adequate protection against infectious diseases. In addition, they are interested in understanding how and why some health conditions, such as pregnancy, obesity and immune compromise, impact on vaccine effectiveness. Researchers are also working to identify both barriers and facilitators to community acceptance of new vaccines.

In 2013, the group's research was centred on clinical trials of the new meningococcal B vaccine; a vaccine which is now licensed and available to provide protection against the most common cause of meningococcal disease. However, the vaccine will not yet be free for all children as the burden of disease and impact from meningococcal diseases in Australian children is not well known. The group will lead a national study to measure the impact of meningococcal disease on children in all states and territories, including Aboriginal and Torres Strait Islander children. This study will provide a detailed comprehensive assessment on the burden of disease from meningococcal disease in children and adolescents, to improve guidelines on the management of IMD cases and will be used by regulatory authorities in Australia and globally to inform meningococcal B vaccine funding decisions.

In 2014, the group will trial new social media and APPS strategies that attempt to improve effectiveness of vaccine uptake in pregnant women and in adolescents to provide better protection against infectious diseases. Helen's group hope to improve timeliness of immunisation in Aboriginal and Torres Strait Islander infants by using a reminder APP to provide earlier and better protection for Aboriginal babies. They are also leading a study to determine what factors affect the immune response to the influenza vaccine in pregnant women, to optimise protection against influenza for pregnant women.



Group members

Research leader: Helen Marshall

Research investigators: Helen Marshall, Christina Boros, Alexia Pena, Mike Gold, Jodie Dodd, Ben Mol and Simon Barry

Clinical researchers: Rachel Chen, Sue Evans, Suja Mathew and Trinh Tran

Academic research manager: Michelle Clarke

Clinical research manager: Chris Heath

Research coordinators: Susan Lee and Jane Tidswell

Postdoctoral researcher: Joanne Collins and Adriana Parrella

PhD candidate: Bing Wang

Research nurses: Christine Heath, Verity Hill, Jane Tuckerman, Mary Walker and Kirsten Zyhajlo

Masters student: Lexa Shrestha and Mark McMillan

Honours student: Nerissa Lakhani



Group members

Clinical researcher: Helen Alvino

Collaborators: Michael Davies, Bart Fauser, Roger Hart, Leonie Heilbronn, Lisa Moran, Rebecca Robker, Ray Rodgers, Helena Teede and Qiao Jie

Professor Robert Norman AO

Reproductive and Peri-Conceptual Medicine, Assisted Reproductive Technology Outcomes

Investigating clinical issues relating to fertility and peri conception health

Peri-conception health is critical to successful fertility outcomes and a healthy baby. The Reproductive and Peri-Conceptual Medicine Group studies a range of important clinical issues which may affect success in fertility and healthy childhood including reproductive conditions such as Polycystic Ovarian Syndrome (PCOS), IVF, weight related fertility as well as general health. They are very engaged in community interactions through activities such as the PCOS Alliance, Your Fertility and a fertility company, FertilitySA.

The main focus for Rob is therefore to:

1. Study the causes, consequences and treatment of PCOS to improve fertility
2. Optimise outcomes of fertility treatments, including IVF
3. Investigate lifestyle and reproductive outcomes before pregnancy in the general and infertility populations

Rob and colleagues are also committed to translating the current NHMRC guidelines they co-wrote for PCOS into clinical practice and are concentrating on optimising ultrasound parameters and modern methods of measuring

testosterone through collaborations with groups in Melbourne, Sydney and Utrecht. The group is also concentrating on appropriate dietary interventions in PCOS and obesity generally, in collaboration with Dr Lisa Moran from the Robinson Research Institute (RRI) and Professor Helena Teede from Melbourne.

Working with Dr Rebecca Robker (RRI), Rob is also seeking to understand the influence of obesity on oocytes and their metabolism. In 2013 several important papers were published on oocyte metabolism and on PCOS and fertility, which identified key pathways, and potential treatments for lipid and dietary induced molecular damage. These interventions are essential to avoid long-term side-effects following fertility treatments in overweight individuals and couples. Rob also works with Associate Professor Leonie Heilbronn (RRI) on long-term metabolic effects of assisted reproduction in adults born following IVF.

Currently, Rob's group is applying for a Centre of Research Excellence in PCOS to develop a country-wide approach to this condition - from basic science to health service delivery.



Group members

Research manager: Leanne Srpek

Research fellow: Ivan Vassilev

PhD candidate: Jared Campbell

Honours student: Ebony Walker

Research assistants: Emmy Bouwman and Stephen McIlpatrick

Collaborators: Peter Cowan, Wayne Hawthorne, Nam Kim, Peter Langendijk and Phillip O'Connell

Associate Professor Mark Nottle

Reproductive Biotechnology

Developing organ and tissue replacement therapies

There is a global shortage of human organ and tissue donors. The Reproductive Biotechnology Group is working alongside a number of interstate and overseas collaborators examining methods to overcome what is one of medical sciences greatest challenges. This multidisciplinary effort is recognised as the leading research of its kind in the world.

The role of Mark's group is to develop various biotechnologies to facilitate this work. As part of this research they are developing the pig as a large animal model for human stem cell research.

In 2013, the group isolated pig embryonic stem cells from parthenogenetic embryos. They also collaborated with Professor Paul Verma from the South Australian Research and Development Institute (SARDI) to induce pluripotent stem cells for the pig. Researchers have now derived all the major stem cell types for the pig, which have been advocated for use in cell therapies for humans.

Professor Martin K Oehler and Dr Carmela Ricciardelli

Reproductive Cancer

Identifying novel biomarkers and therapeutic targets for ovarian cancer

Ovarian cancer is a devastating disease and the leading cause of death from gynaecological malignancies, affecting approximately one in 90 women in Australia. Over 70% of patients present with advanced disease, and despite improvements in surgery and new developments in chemotherapy, ovarian cancer mortality rates have not changed substantially over the last decade. Significant improvement in ovarian cancer survival will require the development of novel ovarian cancer biomarkers for early detection and more effective molecularly targeted therapeutics.

The Reproductive Cancer Group is researching the mechanisms of ovarian cancer metastasis, resistance to chemotherapy, and the identification of novel biomarkers for early detection. In 2013, their group examined the role of a protein annexin A2 in ovarian cancer metastasis.

The group's previous studies identified annexin A2 to be up-regulated in the co-culture ovarian cancer and peritoneal cells. Using in vivo models including the chick chorioallantoic membrane assay and a non-invasive whole-body bioluminescent imaging

xenograft mouse model, the researchers found that annexin A2 plays a critical role in ovarian cancer metastasis and is a new promising therapeutic target for ovarian cancer.

Importantly, they showed that annexin A2 is increased in the blood of ovarian cancer patients compared to normal controls or patients with benign disease. The group also found that a sugar molecule, hyaluronan plays an important role in ovarian cancer chemotherapy resistance. Hyaluronan synthesis by ovarian cancer cells is increased by chemotherapy treatment and high serum hyaluronan levels are associated with reduced progression-free survival and overall survival. Hyaluronan may also regulate the expression of a family of drug transporters (ABC transporters), which are known to be associated with multidrug resistance.

In 2014, the group will determine whether annexin A2 can be used as a diagnostic marker in large independent cohorts of ovarian cancer. They will also assess whether hyaluronan inhibitors are effective in reversing chemo-resistance using established ovarian cancer cell lines and primary cells derived from ovarian cancer patients with chemo-resistant disease.

“Over 70% of patients
present with advanced
disease...”



Group members

Research assistants: Dr Carmen Pyragius, Anita Oehler and Izza Tan

PhD candidate: Noor Lokman

Honours student: Emily Hawkins

Affiliate members: A/Prof Peter Hoffman, Dr Ove Gustafsson, and Dr Florian Weiland

Collaborators: A/Prof Frank Grutzner, Prof Viola Heizelmann-Schwarz, A/Prof Andrew Ruszkiewicz and Dr Andrew Stephens



Group members

Emeritus Professor:
Geoffrey Davidson

Clinical researcher: Rammy Abu-Assi

Research officer: Stamatiki Kritas

Research nurse: Lisa McCall

Consultants: Malcolm Bakewell and
Lisa Ferris

Associate Professor Taher Omari

Gastroenterology

Advancing diagnosis and treatment of common swallowing and gut motility diseases

Swallowing dysfunction (dysphagia) is common in the paediatric population and is a potentially serious medical problem. Current diagnostic assessments use visual evaluation where the swallowing dysfunction can be described, but the underlying mechanisms cannot be objectively measured. The Gastroenterology Group has developed and validated an objective, sensitive and specific method for detecting pressure and flow dynamics during swallowing. The results from this test indicate mechanisms of dysfunction associated with dysphagia that predispose patients to aspiration. These specific and objective measures are used to derive an index of aspiration risk which Taher proposes can complement clinical assessment and guide dysphagia management.

Taher's group undertakes research in common motility diseases, particularly reflux disease and swallowing disorders (dysphagia). The group is widely known for innovating and developing highly accurate measurements of gut motility in patients of all ages. Taher and colleagues also seek to correlate novel physiological measures with clinically relevant outcomes including new diagnostic methods and treatments.

In 2013 the group invented and clinically applied a novel technique, called 'Pressure-Flow Analysis' for the assessment of swallowing function. This new approach has the potential to revolutionise assessment, diagnosis and measurement of changes amongst patients with swallowing disorders as a number of mechanical measures are captured objectively. The technique

derives quantified measures which reliably discriminate different types of swallowing dysfunction and pathophysiology. Taher has now established extensive national and international collaborations utilising Pressure-Flow Analysis techniques and identified the critical variables required for accurate diagnosis of swallowing dysfunction defined by the gold standard of aspiration on videofluoroscopy. The group has undertaken a focused research program to establish the evidence base for use of Pressure Flow Analysis in the paediatric population. They have now unequivocally demonstrated that objective assessment of pharyngeal swallowing using Pressure-Flow Analysis methods is not only a predictor of aspiration risk on fluoroscopy, but also significantly correlates with subjective clinical assessments of dysphagia severity and clinical management of oral intake. This new information, linking objective functional measurements with clinical severity, is unprecedented and clearly demonstrates that we now have the capability to make independent, objective and reliable assessments of swallowing ability.

Taher is now planning the first randomised controlled trial of a management strategy for paediatric dysphagia based on objective functional measures. It will assess the use of Pressure-Flow Analysis to drive decision making for texture modifications and measure the clinical outcomes for children with dysphagia.

Professor Julie Owens

Early Origins of Health and Disease

Preventing developmental programming of obesity, metabolic disease and poor neurological health in offspring



Obesity, diabetes, the metabolic syndrome and cardiovascular disease are amongst the most common non-communicable diseases in Australia and across the world. It is now recognised that the environment before birth and in infancy and childhood, can predispose individuals to later develop these and other health problems. The mother and her nutrition, physical activity and health all affect the intrauterine environment. The presence of a healthy placenta that delivers appropriate nutrients and oxygen to support fetal growth is also critical in this regard. Common pregnancy conditions such as placental insufficiency or obesity cause an adverse intrauterine environment that programs later obesity and cardiometabolic diseases and poor cognition and behaviour.

The Early Origins of Health and Disease Group is increasing our understanding of how these common maternal conditions, particularly placental insufficiency and restricted intrauterine growth, adversely affect the short and long-term health of offspring. The group also aims to identify interventions in pregnancy or early postnatal life to 'rescue' the growth-restricted fetus for improved survival, growth and long-term health outcomes, including risk of obesity and diabetes. In 2013, researchers focused on collecting evidence in experimental models relating to interventions before or after birth to 'rescue' the growth restricted fetus and improve their long-term health. One key finding was that obesity onset in growth-restricted offspring can be prevented with neonatal treatment using a GLP-1 analogue that promotes insulin production. In addition, the group extended the scope to examine the effect of intrauterine growth restriction on other aspects of health. They found that intrauterine growth restriction impairs some, but not all, immune responses in offspring. These findings suggest that therapeutic approaches to overcoming early life programming of obesity and diabetes can be achieved through targeting the insulin production pathways in young offspring and that our models can be used to examine other health outcomes.

In 2014, Julie's group will investigate how effective various interventions during pregnancy or in the neonate are in improving health of intrauterine growth restricted offspring, particularly their metabolic health and also, allergy, cognitive function and behaviour.



Group members

Research leaders: Kathryn Gatford, Julie Owens and Jeffrey Robinson

Senior postdoctoral researcher: Anne Macpherson

PhD candidates: Vincent Chu, Pat Grant, Himawan Harryanto, Dane Horton, Damien Hunter, Wee-Ching Kong, Ezani Mohamed Jamil, Hong Liu, Saidatul Mohammed, Siti Sulaiman, Tulika Sundernathan and Amy Wooldridge

Honours students: Daniel Hodgson and Chloe Douglas

Affiliates: Miles DeBlasio, Marie Dziadek, Bill Hague, Jill Lipsett, Debbie Lawlor, Margaret Morris, Caroline Relton, Rebecca Simmons, Prema Thavaneswaran and Mary Wlodek

Collaborators: Bill Hague, Debbie Lawlor, Glen McConnell, Margaret Morris, Julia Pitcher, Caroline Relton and Rebecca Simmons



Associate Professor David Parsons

Cystic Fibrosis

Developing gene therapy for prevention or treatment of cystic fibrosis (CF); devising X-ray imaging analysis of gene therapy success in living airways

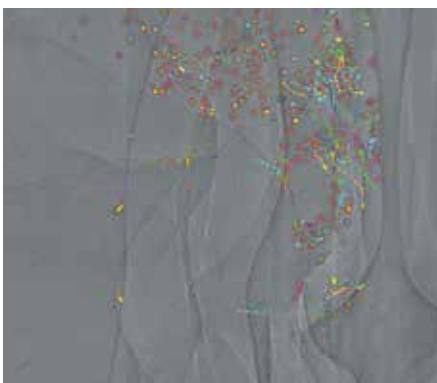
Group members

Postdoctoral researchers: Dr Martin Donnelley and Dr Patricia Cmielewski

PhD candidates: Nigel Farrow, Ryan Green and Harsha Padmanabhan

Honours student: Jahan Penny-Dimri

Administrative assistant: Corrine Reynolds



Cystic fibrosis (CF) is a relatively common chronic and early-fatal genetic disease. It is caused by a faulty gene known as CFTR, which must be inherited from both parents in order for a child to have the disease. In many sufferers it reduces lifespan to young adulthood, mostly through its steady destruction of the lungs and often due to the failure of other organ systems. Given children with CF are born with unaffected lungs that later become infected and inflamed, the group are focused on developing a gene therapy treatment for use in early life to prevent lung disease from establishing or progressing. Success would transform the lives of children with CF, allowing them to live longer and relatively normal lives.

The group is researching lentiviral CFTR vector gene delivery, transduction of airway stem cells in-situ to enable extended gene expression, fast and accurate outcome measurements for assessment of airway disease, and tracking the effects of novel therapeutics using a new type of X-ray imaging.

In 2013, David's group continued to develop their novel synchrotron-based imaging of the effects of physiological changes on airway and lung function. In collaboration with physicists from Monash University and the SPring-8 Synchrotron in Japan, they have published key findings, which detail progress with measurement of airway surface liquid and the clearance of particles that deposit on the airways, critical controllers of airway health. In late 2013, the group began novel experiments studying airflow in mouse lungs using non-synchrotron sources. Visits to the Australian synchrotron and the Japanese synchrotron confirmed the utility of the imaging methods. The group also tested the effect of several pharmaceutical treatments on mucociliary transit and airway surface liquid depth.

In 2014, the group will expand their X-ray based lung function studies and they plan to further investigate mechanisms underlying the success of their airway gene transfer method. They will also compare the relative effectiveness of several gene transfer vectors and gain novel data on airborne environmental lead particle uptake in live mouse lungs. The group continues to develop aerosol delivery methods and automated analysis routines for lung X-ray data.

Dr Julia Pitcher and Associate Professor Mike Ridding

Neuromotor Plasticity and Development (NeuroPAD)

Investigating how early life events such as preterm birth affect the functional development of the brain, its ability to learn and remember throughout life, and its ability to recover from injury or illness in later life

Development of the brain is a life-long process. The human brain adapts based on life experiences and is capable of learning throughout life - an ability called neuroplasticity. For example, in later life, neuroplasticity can help recovery post stroke. However, the brain is at its most 'plastic' in fetal life and during early childhood. Unfortunately, this enhanced early life neuroplasticity also makes the brain highly vulnerable to developmental problems and injury.

NeuroPAD investigates how the functional development of the brain is altered by various early life exposures (eg preterm birth, fetal growth restriction, maternal stress and infection and medical treatments in the neonatal intensive care unit) as well as genetic, epigenetic and postnatal environment factors. Understanding these mechanisms will help the group develop interventions and treatments to improve learning, memory, and cognitive and motor function in vulnerable populations. It will also help to prevent unintended injury in clinical practice and will help patients at all stages of life recover from brain injury.

The group is examining how the development of the brain's cortex is affected by being born preterm and/or growing poorly in utero. While the group's brain stimulation techniques can be used to induce and measure plasticity experimentally, there is a global research effort to try and develop these techniques as therapies for neurological disorders where neuroplasticity is affected. Such disorders include functional recovery from stroke, writer's cramp, tinnitus (ringing in the ears) and drug-resistant depression. The group has also been developing and refining novel non-invasive brain stimulation techniques for inducing functionally beneficial neuroplasticity in targeted brain regions. They have started

work to see if these techniques are also useful in reducing symptoms in conditions typified by chronic pain, and for rehabilitation after stroke. These techniques may also prove useful in improving motor and cognitive outcomes in preterm children.

In 2013 the group developed a novel non-invasive brain stimulation approach that can induce robust plastic change within the brain. Conventional stimulation paradigms can only induce very short lasting changes in the brain that reflect the very earliest stages of processes important for learning and behaviour. Recent PhD graduate Mitchell Goldsworthy provided evidence that the changes induced with our newly developed technique are due to the engagement of later phase mechanisms of neuroplasticity. This finding is important because these later phase mechanisms are likely to be very important for behaviour and rehabilitation. We are now developing this approach further and testing its capacity to modify behaviour. These studies will underpin the development of novel therapeutic approaches for the rehabilitation of neurologically impaired individuals.

In 2014 the group has two key focuses. Firstly, the group is investigating the role of altered stress hormone responsiveness and epigenetic changes in the learning and memory difficulties of a large new cohort of preterm children. Secondly, the group is part of an international multi-centre trial that is researching the best time to begin rehabilitation in stroke patients as well as developing non-invasive brain stimulation techniques for rehabilitation.



Group members

Postdoctoral researchers: Luke Schneider and Ann-Maree Vallence

Research fellow: Nicolette Hodyl

Clinical researchers: Michael Stark and Nicholas Smith

Research officer: Ruiting Yang

PhD candidates: Sam Darvishi and Mitchell Goldsworthy

Research nurses: Ros Lontis and Louise Goodchild

Research assistant: Rohan Meigel



Group members

Research fellows: Tina Bianco-Miotto

Postdoctoral researchers:
Amanda Highet and Sean O'Leary

PhD students: Jessica Laurence,
Shalem Leemaqz, Sam Buckberry,
Dee McCormack and Alison Leviton

Research assistant: Dylan McCullough

Masters student: Sultana Khoda

Honours student: Fleur Spronk

Affiliate: Denise Furness

Collaborators: Lesley McCowan, Robyn North, Louise Kenny, Lucilla Poston, Jenny Myers, Phil Baker, Jimmy Walker and Nigel Simpson from the SCOPE Consortium, Eugenie Lumbers, Kirsty Pringle, Paul Anderson

Professor Claire Roberts and Professor Gus Dekker

Placental Development

Understanding placental development and maternal adaptation to pregnancy and their roles in pregnancy complications

More than one quarter of pregnancies in Australian women are associated with pathologies of the placenta which result in miscarriage, preeclampsia, intrauterine growth restriction, preterm birth, unexplained stillbirth and placental abruption. These conditions are believed to stem from impaired placental invasion and inadequate physiological transformation of the uterine spiral arteries to ensure appropriate maternal blood supply to the placenta. There are currently no reliable clinical assessments available to determine which women are at risk of these conditions. As a result, adverse pregnancy outcomes due to placental pathologies often cannot be prevented. This is particularly an issue for first pregnancies, where no prior history can be used to predict poor outcomes.

The Placental Development Group conducts cellular and molecular research to elucidate mechanisms that govern normal and abnormal placental development. This understanding informs prediction of pregnancy outcome and will enable future interventions to prevent or ameliorate pregnancy complications.

In 2013 researchers identified single nucleotide polymorphisms in mother, father, baby trios that together with clinical, dietary and lifestyle factors predict pregnancy complications. They also studied the role of vitamin D in placentation and pregnancy outcome, using human and mouse studies. Additionally the group researched the role of hypoxia in early placental differentiation and investigated sex differences in the human placental transcriptome.

Claire's and Gus's group has a strong focus on identifying genetic, nutritional, lifestyle and clinical factors that associate with pregnancy outcome. These studies are ongoing, and conducted in well-described pregnancy cohorts.

Research is increasing our understanding of how pregnancy complications develop, and is identifying factors that place women at risk. Some of these factors may be amenable to intervention in the future.

Professor Sarah Robertson

Reproductive Immunology

Defining the immune pathways to healthy conception and pregnancy

Pregnancy is a unique situation where the foreign tissues of the fetus and placenta develop within the female body, despite direct contact with the female immune system. To enable healthy pregnancy, an active state of immune adaptation and tolerance must occur.

The Reproductive Immunology Group aims to:

1. Understand the process by which maternal immune cells achieve immune adaptation to allow pregnancy to commence
2. Determine how the cytokine balance at conception affects embryo implantation and quality, to program placental growth and fetal development
3. Define how paternal factors contributes to these reproductive events
4. Understand how inflammation affects fertility and pregnancy success

In 2013, Sarah's group explored how special immune cells known as regulatory T cells are generated at the time of conception, to mediate the immune tolerance necessary to allow implantation of the embryo and allow healthy placental function. The group has shown that seminal fluid drives activation of regulatory T cells by provision of key signals including immune-regulatory cytokines and Toll-like receptor ligands. Using microarray strategies, studies are demonstrating a novel role of microRNAs induced by seminal fluid exposure, in controlling tolerogenic dendritic cells and eliciting the correct T cell response.

These paternal signals can influence progression of pregnancy and affect the health of progeny after birth.

In a novel mouse model system allowing investigation of the effects of repeated seminal fluid exposure before pregnancy, the group is concentrating on defining how each exposure acts to boost the strength of the regulatory T cell response, which begins to explain why duration of sexual cohabitation is a factor in immune pathologies of pregnancy such as preeclampsia. Importantly, progesterone is a crucial factor in developing an adequate T cell response, and the group's recent work has defined how progesterone synthesis at conception depends on immune cells in the ovary, notably the pro-angiogenic actions of macrophages in the corpus luteum.

In a related stream of work, Sarah's team is exploring how the inflammatory response controls the timing of labour and is investigating how various anti-inflammatory interventions, including strategies to inhibit Toll-like receptor signalling and/or to promote regulatory T cells, may be efficacious in preventing preterm labour. An emerging focus is how inflammatory insults such as infection, obesity or diabetes can alter the immune environment and affect conception and pregnancy, and potentially contribute to pathways resulting in placental dysfunction causing fetal growth restriction and pre-eclampsia.



Group members

Research fellow: Kerrilyn Diener

Senior postdoctoral researcher: David Sharkey

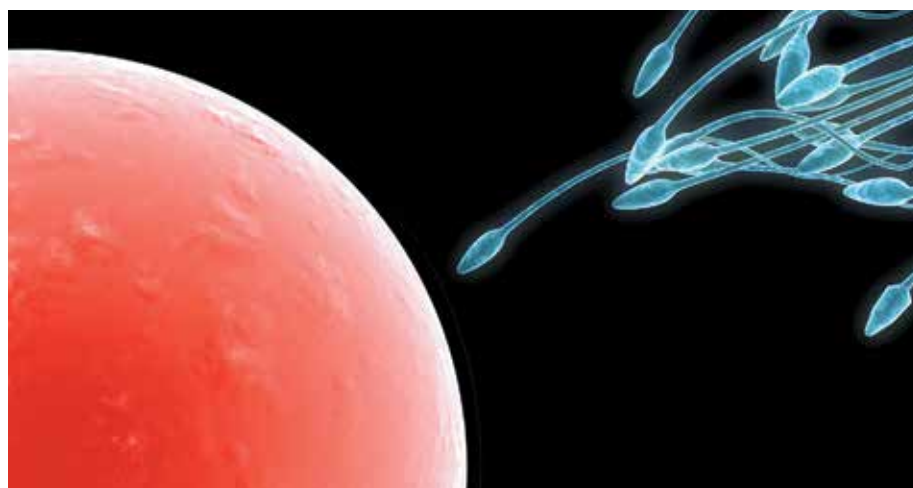
Postdoctoral researchers: Alison Care, Nardhy Gomez-Lopez and John Schjenken

Research officer: Camilla Dorian

PhD candidates: Peck Chin, Mohammad Johan, Jelmer Prins and Hanan Wahid

Honours students: Andrew Lobb and Bihong Zhang

Visiting scientists: Min Jin and Sabine Segerer





Dr Rebecca Robker

Ovarian Cell Biology

Investigating cellular mechanisms driving ovulation and embryo development

Group members

Postdoctoral researchers: Lisa Akison and Linda Wu

Clinical researcher: Robert Norman

PhD Candidates: Victor Chen, Macarena Gonzalez, Astrud Tuck and Siew Wong

Research assistant: Jamie Zhang

Ovarian function is at the core of many aspects of women's health. The ovary nurtures oocytes: endowing them with the building blocks they need post-fertilisation and releasing them at precisely the right time. The ovary also produces the hormones that coordinate the oviduct and uterus to transport and receive an embryo. Discovering the molecular mechanisms that control these ovarian processes is essential for understanding the very basics of female fertility in all mammalian species.

Infertility affects one in six Australian couples and is often due to a lack of healthy oocytes or an inability to ovulate a fertilisable egg. For instance, an estimated 8% of Australian women suffer from polycystic ovary syndrome in which they are predisposed to obesity and insulin resistance and their ovarian follicles grow but fail to ovulate. Conversely, millions of women take hormones daily to prevent ovulation. Obesity further complicates the biology of ovulation and pregnancy, especially in Australia where obesity rates are amongst the highest in the world. Ectopic pregnancy can result if transport of the fertilised oocyte does not progress normally through the oviduct.

The Ovarian Cell Biology Group is working to provide new knowledge and a better understanding of ovarian biology and the ways in which it can go awry in various infertility disorders. The team is investigating how the metabolism of lipids is regulated in oocyte complexes and how excess fat

changes its capacity to form an embryo. They are also investigating the basic biology of the oviduct in order to understand how it nurtures embryos and influences their healthy development during the earliest stages of pregnancy.

The group has discovered that the process of β -oxidation lipid metabolism is tightly regulated in oocyte complexes and that when oocytes are matured using in vitro procedures this type of metabolism is not properly activated. They also found that exposure of the oocyte complexes to insulin-sensitisers that are used in the treatment of type-2 diabetes reduced β -oxidation and was detrimental to embryo development.

Two new PhD students commenced their research projects in the lab and are identifying specific cellular changes in oocytes of obese mice and trialling novel treatments to improve the quality of these oocytes so that they have the capacity for improved embryonic and fetal development, and thus a healthier start to life.

Using microarray analysis of oviducts from mice lacking the progesterone receptor the group was able to identify and characterise the expression of progesterone target genes in the oviduct that are likely to have important roles in sustaining and transporting the embryo during the first few days of life.

Professor Ray Rodgers

Ovarian Developmental Biology

Understanding the role of the ovary in fertility and endocrine function

In addition to its central role in fertility, the ovary affects many other physiological systems in women and plays a role in systemic disease. One very common disorder involving the ovary is Polycystic Ovary Syndrome (PCOS), affecting approximately one in 20 women of reproductive age.

Affected individuals suffer infertility symptoms of excess androgens and they are predisposed to becoming obese and developing type-2 diabetes and dyslipidaemia. It is not simple to diagnose and its causes are not well understood.

The Ovarian Developmental Biology Group seek to understand how the ovary functions, what can go wrong, when and why. They expect their research will help develop better treatments and strategies for prevention of infertility and PCOS.

In 2011 studies suggested that the biological predisposition to developing PCOS is established in the fetal ovary. In studying the fetal ovary, researchers identified that the prevailing theory on how the ovary develops and the origins of some of the cell types is not correct. They proposed a new model and identified a novel precursor somatic cell in the fetal ovary.

Ovaries of PCOS women produce more androgens than normal ovaries. In a long-term collaboration with Phil Knight and Ross Bathgate, the group identified the role of a molecule INSL3 in regulating the gene encoding the enzyme that is key for producing androgens in the ovary.

The group plans to study the regulation of genes in fetal ovaries that are associated with PCOS and to explore the pluripotential of fetal somatic cells.



Group members

Research assistants: Wendy Bonner, Nicholas Hatzirodos and Yvonne Miels

PhD candidate: Katrina Copping

Postdoctoral researcher: Katja Hummitzsch

Honours student: Isabella-Rose Meredith

Collaborators: Richard Anderson, Ross Bathgate, Phil Knight, Lisa Martin, Dieter Reinhardt and Dagmar Wilhelm



Group members

Postdoctoral researchers: Lisa Akison and Kylie Dunning

Research officer: Laura Watson

Research assistant: Jamie Zhang

PhD candidates: Tan Izza and Adrian Kaczmarek

Associate Professor Darryl Russell

Ovarian & Reproductive Cancer Cell Biology

Defining the molecular mechanisms of hormone control of ovarian folliculogenesis

Infertility and endocrine diseases frequently originate from dysfunction of the ovary. To achieve normal fertility and the healthy development of fertilised embryos, the ovary must produce high quality oocytes. The Ovarian and Reproductive Cancer Cell Biology Group is focussed on understanding the unified mechanisms by which hormone signals and tissue structure determine the health and function of ovaries. The group aims to harness this knowledge to improve reproductive health and advance treatments for infertility and diseases such as Polycystic Ovarian Syndrome (PCOS) and cancer.

Recent work has identified an important new molecular aspect of the communication between oocytes and the ovarian somatic cells. Signalling molecules released by the oocytes act through specific structures in the ovarian extracellular matrix. Female hormones discretely modify these structures establishing an information

rich interaction between the maternal endocrine and oocyte systems. This promising work has received new NHMRC project grants, commencing in 2014.

Drawing on insights from the ovary, Darryl's group also showed a related mechanism at work in reproductive cancers. They found that growing tumours use similar strategies to modify extracellular matrix structures and modify interaction between the tumour and host. This allows tumours to attract a blood supply and suppress host defences to block cancer growth. The result is progression to metastatic spread - the most lethal form of this disease.

Darryl's ongoing research focus is to build exciting novel discoveries that advance new therapeutic approaches to prevent infertility and refine new non-hormonal contraceptive technologies. Diagnostics and therapeutics to block cancer spread are also emerging through new insights in cancer metastasis.



Group members

Postdoctoral researcher: Lauren Miller-Lewis

PhD candidate: Sara Pfeiffer, Amy Kaim

Project officer: Jenny Clark

Research assistants: Olivia Carger, Amy Kaim, Christine Mpundu-Kaambwa, Jacqueline Peters, Christy Reece, Richard Sprod

Affiliate: Lauren Miller-Lewis

Admin officer: Robyn Clements

Professor Michael Sawyer

Research and Evaluation Unit

Developing and evaluating new population-level interventions for the health and wellbeing of mothers and children

Optimal physical and mental health is an important ingredient for strong and resilient communities. Many mothers and children however experience sub-optimal levels of health and wellbeing. For example, approximately 13% of new mothers experience significant symptoms of depression, while at any single point of time 14% of children and adolescents experience mental health problems. What is also concerning is the repeated finding that only a minority of those with problems receive help from professional services. There is a strong need to develop new cost-effective interventions that will improve the health and wellbeing of mothers and their offspring in the general community. Staff in the Research and Evaluation Unit are working closely with clinical staff in the community child health service in South Australia to develop and evaluate new population-level interventions that have the

potential to improve the health and wellbeing of mothers and children. The effectiveness of these interventions is assessed in clinical trials that are conducted as part of routine service delivery in the community child health service.

In 2013 Michael and colleagues completed the development of a new intervention (the 'eMums' program) that combines the professional skills of community nurses with the capacity of the internet to reach large numbers of mothers in the general population. The effectiveness of this intervention is currently being evaluated by means of a randomised controlled trial conducted within the community child health service in South Australia.

In 2014 Michael will continue the randomised controlled trial and will refine the 'eMums' intervention using experience gained to date – with the aim to seek grant funding to enable an evaluation of this refined program.

Dr Quenten Schwarz

Neurovascular Research

Understanding the molecular mechanisms controlling neuronal and vascular development

Understanding development and integration of the neuronal and vascular systems at the molecular level presents a major challenge to developmental biologists. Recent advances, including our own, conclusively show that similar molecules are used by both systems to coordinate their development.

The Neurovascular Research Group is particularly interested in understanding the signalling pathways controlling neural stem cell development with the aim of identifying molecular defects underlying neurodevelopmental disorders including neuronal tumours, neurocristopathies and neuropsychiatric illness. Together, these disorders affect over 5% of the population and arise from aberrant neuronal development.

The group have recently identified several key signalling molecules in neuronal development and are now using genome-wide studies in association with an array of animal models to characterise the function of these proteins in neuronal migration, stem cell maintenance and differentiation.

The group experienced several seminal findings that led to breakthrough publications in 2013. They provided the first documentation for an E3 ubiquitin ligase in neural crest cell and craniofacial development. This finding identified a novel role for ubiquitination in stem cell maintenance and survival that has implications for stem cell biology in general. They also found an essential role for the protein 14-3-3zeta in dopaminergic signalling, the key pathway that is perturbed in mental disorders such as schizophrenia and autism. They further showed that 14-3-3zeta modulates activity of the dopamine transporter DAT, which is a major site of drug therapy. The implications of this finding provide hope in identifying further avenues of treatment for psychiatric disorders.

In 2014 the group is pursuing the roles of Nedd4 in neural crest cells to identify novel molecules controlling craniofacial development. In addition they are exploring the mechanisms through which 14-3-3zeta controls DAT function as a means to identify novel drug targets.



Group members

Postdoctoral Researcher: Peter McCarthy and Sophie Wiszniak,

Research Assistant: Samueala Kabbara and Xiangjun Xu

PhD Candidate: Zarina Greenberg, Rachael Lumb and Eiman Saleh

Collaborators: Christiana Ruhrberg, Julian Heng, Maarten van den Buuse and Bernhard Baune



Group members

Postdoctoral Researchers: Kristie Lee and Shervi Lie

PhD Candidates: Tessa Mattiske and May Tan

Honours Student: Kelsey Ireland

Research Officer: Susan Hinze

Research Assistant: Ching Moey

Associate Professor Cheryl Shoubridge

Molecular Neurogenetics

Investigating the molecular mechanisms and functional impact of mutations in genes causing X-linked intellectual disability with a goal to assess molecular targets for therapeutic intervention

The brain is the most complex organ in the body. Intelligence describes the brain's ability to process and comprehend information, infer and decision make, give capacity to reason, use language as well as plan and learn. These cognitive abilities require correct anatomical set up during development and the continued ability to adapt to and respond to physiological cues. Disruption to any of these elements can lead to deficits in cognitive abilities.

Intellectual disability is defined as significantly impaired cognitive functioning coupled with a deficit in adaptive behaviour with onset before age of 18. Intellectual disability is frequent in the population with as many as one in every 50 people in the world affected. The annual cost to Australia of intellectual disability is estimated at \$14 billion.

The goal of the Molecular Neurogenetics Group is to generate knowledge of the crucial components of neuronal homeostasis through identification and functional characterisation of naturally occurring human mutation leading to abnormal cognitive outcomes. This is essential for a better understanding of brain function and paves the way for design of highly sought after treatment strategies.

Cheryl's group have mice modelling two frequent mutations in a gene mutated in X-linked intellectual disability that is involved in the correct set up of specific neurons in the developing brain. They have shown that pathogenesis of these mutations is linked to a marked reduction of mutant protein expression in specific regions of the brain during early embryonic development. What is still unclear is how different mutations in this gene contribute to the substantial clinical variability seen in patients.

Another intellectual disability gene the group is modelling involves the adaptive ability of the brain including dynamic structural changes required for neuron communication. Using primary neurons in cell culture they have begun to establish the impact of these mutations on these neuron structures.

The group's research will address the functional impact of naturally occurring mutations in genes involved in intellectual disability in models relevant to the neuronal setting of the associated clinical phenotypes. This work will define the developmental deficits at the cellular level and provide direct evidence of the components of the pathways implicated in disruption to cognitive abilities and seizures.



Associate Professor Michael Stark

Neonatal Medicine Research

Improving the long-term health of premature and seriously ill newborns

Events, illnesses and treatments in the newborn period can have profound and long-term deleterious effects on growth, development and general health.

The Neonatal Medicine Research Group addresses four main themes:

- > Generating evidence relevant to care of the compromised newborn
- > Bringing basic science to the bedside to aid and assist care
- > Critically appraise current practice and identify evidence gaps
- > Building collaborations with research partners in South Australia as well as nationally and internationally

In 2013 further advances were achieved in nutrition of babies born pre-term, not only towards improving physical growth but also

improving development and cognition. On a physiological level, researchers have focused on control of oxygenation and circulation especially of the brain and gut, and the role of transfusion, specifically transfusion related immunomodulation in the pathophysiology of common neonatal morbidities. Collaboration with materno-fetal medicine has continued with detailed follow ups of babies whose mothers were enrolled in fetal therapy and intervention trials.

2014 will see further progress in nutritional studies. Researchers will also investigate the impact of cerebral oxygen kinetics on neuro-developmental and long-term developmental outcomes following preterm birth.



Group members

Research Leaders: Chad Anderson, Ross Haslam, Andy McPhee and Michael Stark

Postdoctoral Researcher: Vicki Xafis

Affiliate Members: Nicolette Hodyl

Collaborators: Carmel Collins, Caroline Crowther, Nicolette Hodyl, Robert Gibson, Julia Pitcher, Phillipa Middleton and Maria Makrides

Professor Paul Thomas

Neural Development

Understanding the genetic basis and pathology of disorders that affect the reproductive and central nervous system

The Neural Development Group focuses on the genetic causes of reproductive and neurological abnormalities, which are among the most common health conditions in children.

The group have established mouse models for neurological disease genes, which are providing unique insights into the genetic control of brain development and the biological basis of mental retardation and epilepsy. They have also established a unique mouse model of sex reversal in which chromosomally female mice develop as males. These mice are providing exciting new insights into the evolution and molecular mechanism of sex determination in mammals.

In 2013 the group developed a new technology termed genome editing which enables them to quickly and inexpensively establish mouse models for reproductive and neurological disorders. It is believed they are the only group in Australia to have successfully used this technology to generate gene knock-out mice.

In 2014 Paul's group plan to establish the SA Genome Editing (SAGE) facility, which will be part of the group of Institute's Core Facilities. This will enable members to rapidly generate mouse models for their research projects.



Group members

Research Fellows: Bryan Haines and James Hughes

PhD Candidates: Dale McAninch, Nicholas Rogers, Fatwa Adikusuma and Daniel Pederick

Research Officer: Sandie Plitz



Group members

Postdoctoral Researchers: Hannah Brown and Melanie McDowall

Research Assistants: Marie Anastasi, Lesley Ritter and Melissa White

Technical Assistant: Anwar Fatohi

Affiliate: Karen Kind

Collaborators: Andrew Abell, Jose' Buratini (Brazil), Pablo Cetica, Gabriel Dalvit (Argentina), David Gardner, Robert Gilchrist, Mariana F Machado (Brazil), Tanya Monro, David Mottershead, Darryl Russell, Rebecca Robker and Sarah Robertson

Associate Professor Jeremy Thompson

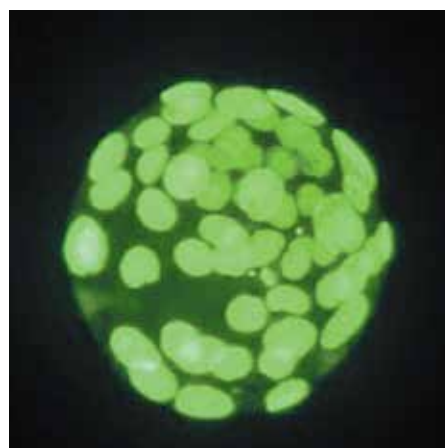
Early Development

Understanding the link between altered metabolic states within oocytes and embryos and epigenetic mechanisms controlling growth

Fertilisation causes dynamic molecular and biochemical changes to both egg and sperm. We now know that the maternal metabolic environment in which fertilisation takes place can have a major impact on subsequent embryonic and fetal development leading to altered adult health. The newly fertilised egg is extremely sensitive to the microenvironment within the maternal reproductive tract, and this is reflected in a process of 'resetting' its epigenetic code. If the metabolic microenvironment surrounding the oocyte and embryo is altered as a result of diet and lifestyle factors, this will influence the epigenetic mechanisms that ultimately control the growth rate and development potential of the resulting fetus.

The Early Development Group explores the metabolic and epigenetic consequences of environmental stress (e.g. in vitro culture, hyperlipidemia and hyperglycaemia) on the earliest stages of embryo development. Work spans the impact of diet in dairy cows to the tightly regulated events of the transitioning chromatin of the maturing oocyte and early embryo. Jeremy's team are using multi-disciplinary approaches to answer questions about the contribution of the peri-conception period to health. The group's major focus is to explain the direct mechanisms by which environmental stress impacts early development, to develop new tools to measure the changes, and to successfully develop interventions to reduce the impact.

In 2013, new and existing collaborations with chemists and physicists at the University of Adelaide, saw the development and use of a number of new and novel technologies and techniques designed to better understand the mechanisms of perturbed embryo development. The group has the advantage of a new microscope that images fluorescent markers to assess the impact of both ionic flux (calcium) and production of damaging substrates (such as hydrogen peroxide) within the oocyte and early embryo during the early developmental period in real time, using time-lapse imaging.



The announcement of a large collaborative ARC CoE in late 2013 means that developments in nanosensing ionic and metabolic changes within the oocyte and early embryo are likely to increase exponentially in the coming years. 2013 also saw major progress in their work on the impact of maternal hyperglycaemia (diabetes) on epigenetic reprogramming of the oocyte and early embryo via the addition of modified glucose molecules to nuclear proteins (O-linked glycosylation). Building on their existing data, they have recently discovered that dramatic changes occur to the core chromatin of mature oocytes in response to hyperglycaemic conditions. This is the first example of a direct mechanism by which diabetes affects programming in the oocyte.

In 2014 the group's research focus is to refine and develop new sensing and visualisation tools to detect the metabolic and epigenetic changes resulting from environmental stress.

Professor Stephen Worthley

Cardiac Repair

Studying and treating cardiovascular disease and related conditions

Cardiovascular disease (CVD) is the biggest cause of mortality globally. The Cardiac Repair Group focuses on a broad range of CVD's and their pathology, management and prevention. These include investigations into CVD in the context of obesity, diabetes, hypertension, and renal failure. Other studies investigate cardiovascular conditions such as coronary artery atheroma (plaque disease), cardiomyopathy, congestive heart failure, structural abnormalities, and aortic valve disease.

The group aims to enhance understanding of the disease process – such as atherogenesis – which will assist in identifying patients at most risk from subsequent adverse events. They also aim to develop more effective and less invasive therapies that will reduce their impact and morbidity on patients, shorten hospital stays and improve outcomes and quality of life.

The group completed the first-in-man trial evaluating intra-vascular radio frequency ablation of renal artery sympathetic nerve fibres for the treatment of resistant hypertension. Researchers commenced novel angiographic studies, which incorporates baseline and follow up intra-vascular near infrared spectroscopy to analyse and monitor coronary atheroma plaque compositional changes and reconcile these with changes in coronary artery endothelial function. The group continued trans-aortic valve implant procedure (TAVI) studies in which prosthetic aortic valves can be introduced and deployed percutaneously, often as an alternative to open-heart surgery. They also continued pre-clinical studies to generate novel data relating optimal timing and dosage of pluri-potent stem cell therapy for the treatment of myocardial infarction.

In 2013 Stephen's group built considerably on previous work with 17 studies submitted and published. These included results of a novel TAVI aortic prosthetic repositionable valve (Lotus) system (REPRISE I Trial), Safety and efficacy of a multi-electrode renal sympathetic denervation system in resistant hypertension (EnligHTN I Trial), further investigation into novel interventional devices and technologies, (e.g. sirolimus-eluting CD34 antibody coated stent to address late in-stent stenosis) and results of a pre-clinical study on impact of timing and dosage of mesenchymal stem cells in an established rat model of myocardial infarction. Further investigative studies were undertaken into the use of CT and MRI in the diagnosis, monitoring and management of heart conditions and structural abnormalities viz; transluminal attenuation gradient in coronary CT for identification of coronary artery stenosis, and cardiac MRI in the diagnosis and surveillance of thoracic aorta perigraft seroma and its complications.

Stephen is also building on previous clinical and pre-clinical studies with further focus on intra-vascular imaging modalities including intra-vascular ultrasound with co-registered spectroscopy, optical coherence infrared imaging (OCT) and fractional flow reserve protocols without the need for hyperaemic agents.



Group members

Senior Research Fellow: Angelo Carbone

Senior Lecturer: Matthew Worthley

Research Fellows: Adam Nelson and Luay Samaraie

Cardiology Fellow: Mitra Shirazi

Interventional Fellows: Anthony Pisaniello and Shweta Sahay

Cardiology Consultant: Karen Teo

Senior Cardiology MRI Radiographer: Kerry Williams

Cardiology MRI Radiographer: Ben Koschade

Clinical Trials Coordinator: Peta King, Joanne Nimmo, Ashley Roach

PhD Candidates: Tim Ballie, Ramesh Chokka, Sinny Delacroix, Lachlan Frost, Rishi Puri, James Richardson, Ararism Shah, Samuel Sidharta and Dennis Wong

Research Student: Victoria Cox

Administrative Assistant: Angela Hooper



Professor Andrew Zannettino

Myeloma Research

Identifying genetic markers and novel therapeutic targets for myeloma

Group members

Postdoctoral Scientists: Stephen Fitter, Duncan Hewett

Research Fellows: Stanley Chueng, Sally Martin, Jacquie Noll and Kate Vandyke

Technical Staff: Vicki Wilczek

PhD Candidates: Chee Man Cheong, Catherine Gan, Natalia Martin, Mary Matthews, Krzysztof Mrozik and James Richardson

Honours Students: Rachel Bala, Ankit Dutta and Tony Le

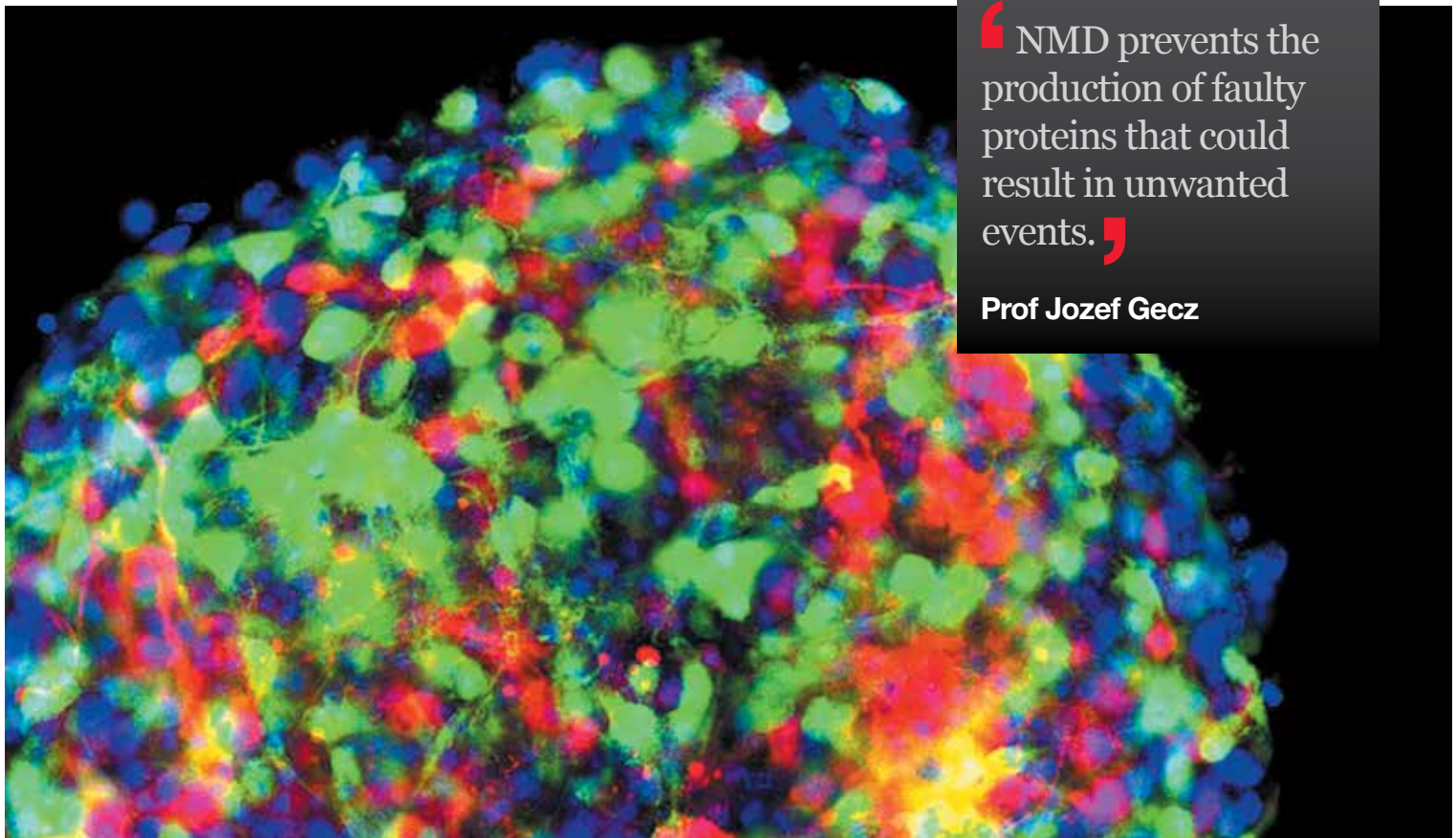
Myeloma is the second most common blood cancer affecting humans, with over 1,500 Australians diagnosed each year. Despite recent advances in treatment, myeloma remains almost universally fatal with a 10 year survival rate of approximately 17%. Myeloma is characterised by the clonal proliferation of malignant plasma cells (an immune cell type that normally protects us against infection). The main clinical manifestations of myeloma are the development of osteolytic bone lesions, bone pain, hypercalcaemia, renal insufficiency, suppressed immunoglobulin production and increased BM angiogenesis (blood vessel formation). It is now widely accepted that most, if not all, cases of myeloma are preceded by a premalignant (asymptomatic) monoclonal gammopathy of uncertain significance (MGUS) stage. However, the genetic factors which trigger the progression from this asymptomatic stage of the disease to overt malignant myeloma remains to be determined. Moreover, recent studies suggest that the bone marrow microenvironment plays a central role in disease progression.

The Myeloma Research laboratory studies the molecular and cellular basis for the development of the bone marrow cancer, multiple myeloma (MM). The laboratory's research is focussed on identifying the key genes which are responsible for disease progression and the role played by the bone microenvironment in disease pathogenesis. Andrew believes that these approaches will enable us to identify new molecular markers of disease risk and to design drugs against novel therapeutic targets.

Key research outcomes for 2013:

- > Identification of a novel tumour suppressor gene which plays a central role in triggering the progression from asymptomatic MGUS to overt malignant MM
- > Defining the role of the bone marrow microenvironment in the development MM
- > Determining the effects of myeloma plasma cells on mesenchymal stem cell (MSC) differentiation
- > Identifying the role of the mTOR pathway in mesenchymal stem cell biology and bone formation





“NMD prevents the production of faulty proteins that could result in unwanted events.”

Prof Jozef Gecz

Quality control in protein production ensures normal brain development

A precise control system known as non-sense mediated mRNA decay (NMD) exists in cells to make sure only top quality proteins are produced.



In 2013 Professor Jozef Gecz and colleagues demonstrated that NMD plays a crucial role in normal brain development, and alterations

in NMD genes were strongly associated with neurodevelopmental disorders. These findings suggest that NMD may one day be the target of therapies to restore normal cellular protein production in the brain and other organs.

“The process of NMD is a very important regulator of normal gene expression and cell regulation,” explained Jozef.

“NMD prevents the production of faulty proteins that could result in unwanted events as tissues are formed. It’s a complex process, and we’re only at the beginning of unraveling its many layers of involvement in the brain and other aspects of human development.”

A number of molecules are involved in NMD, but two of the most important of these are UPF3A and UPF3B. During 2013, Jozef and colleagues investigated whether other NMD molecules are also important for brain development and how NMD actually controlled brain growth. They published evidence from two of their studies in the *Journal of Human Molecular Genetics*.

In the first study, Lam Nguyen – a PhD student – looked at NMD genes in patients, including those with known neurodevelopmental syndromes and others presenting with a range of characteristics including speech delay, hearing impairment, ADHD and sensory problems.

“In addition to UPF3B, we discovered UPF3A and another four NMD genes for which variation in their gene copy numbers was significantly associated with neurodevelopmental disorders,” said Jozef.

“It showed us for the first time that not just one, but indeed a number of these mRNA policing molecules are important for normal development in the brain.”

In the second study, Jozef’s colleague Dr Lachlan Jolly looked at the importance of NMD in immature brain cells known as neural progenitor cells. The study showed that UPF3B and the NMD process itself are tightly controlled, being switched on and off to varying degrees over the course of neural progenitor cell development.

“UPF3B seems to be important for promoting cell specialisation and growth of neurites, the cellular arms which mediate connections between brain cells,” explained Jozef.

Taken together, the new evidence strengthens Jozef’s hypothesis that growth and specialisation of brain cells relies on a balanced system of NMD being in place. It’s a good starting platform from which to launch further studies, and not just those that involve brain development.

Jozef and his colleagues were awarded an NHMRC Project Grant in 2013 to continue their research to determine the roles of NMD in normal cellular development and function in the brain.



“...we could theoretically prevent the onset of type-1 diabetes.”

A/Prof Simon Barry

Arming the body's police

The immune system is the bedrock of our health and when it is compromised the results can be catastrophic.

Associate Professor Simon Barry, who is head of the Molecular Immunology Group, is mapping out a prototype of a healthy immune system, and is closely examining the function of regulatory T cells (Tregs), which play a crucial role in controlling immune function and preventing autoimmune disease. In 2012, Simon discovered the PI16 molecule, a component of Tregs that seems to be a significant differentiator between a healthy immune system and a harmful one.

“We are characterising human Treg cells using the genetic biomarker, PI16 which we discovered using genomics approaches, and which appears to be a marker of stable Treg cells and a healthy immune system,” Simon said.

“Now we’re thinking about bigger ambitions including cell therapy. In other words, completely repairing the immune system in the event of autoimmune conditions. We will transfer cells expressing this molecule back into the patient, with the aim to establish control and reset the immune system.”

The implications of such an advance would be vast; immune system failure is a significant component in many autoimmune diseases including type-1 diabetes, multiple sclerosis, rheumatoid arthritis, as well as chronic conditions including kidney disease and HIV infection. Treg cells are essential for healthy pregnancy and too few Tregs is a cause of many pregnancy disorders. The immune system also poses significant threat to anyone who has received an organ transplant as the body may reject the organ

at any given moment. A cell therapy that restores the immune system may benefit millions of people.

“In a person with type-1 diabetes the immune system attacks the pancreas and the pancreas stops producing insulin. When this happens the person is insulin-dependent and presents with diabetes. By this late stage, the immune destruction is over. If we were able to intervene before the pancreas stops producing insulin, we could theoretically prevent the onset of type-1 diabetes.”

Other researchers have shown that injecting a diabetic mouse with Tregs stops the immune attack and prevents the pancreas from failing. Simon hopes that similar therapies can be developed for humans who have type-1 diabetes and other autoimmune diseases.



“We hope this data will rapidly translate into improved clinical care.”

A/Prof Michael Stark

Understanding and interpreting the origins of early intraventricular hemorrhage

Early intraventricular hemorrhage (IVH) can have lifelong consequences including abnormal neurodevelopment, cognitive impairment, and learning disorders.

Preterm babies are at greater risk of early IVH in the first hours of life, a risk that heightens with lower birth weight and gestational age. Historically, understanding of how to identify those preterm babies at highest risk has been limited. The Neonatal Medicine Research Group, headed by Associate Professor Michael Stark, have been using new technologies to research the roles of oxygen and blood supply to the brain in early IVH. Already, they have expanded understanding of the multi-factorial and complex origins of early IVH. Their hope is that doctors will be better placed to identify high-risk cases and engage in preventative therapies.

Michael, who is a staff specialist in the Department of Neonatal Medicine at the Women's and Children's Hospital, explains why defining the roles of blood and oxygen supply is significant:

“Even within that group of highest-risk babies there are those that come through unscathed and those that develop injury. We don't have a very good predictive tool to identify which ones are at the highest risk. The purpose of this research was to use Near Infrared Spectroscopy (NIRS) to measure the supply of blood and oxygen to the brain,” he said.

One of the benefits of using NIRS to monitor preterm babies is that it provides real-time, non-invasive information about the balance of oxygen delivery and demand in the very preterm brain. Funds provided by Channel 7 and the Women's and Children's Research Foundation enabled the purchase of a new, state-of-the-art NIRS monitor. With this monitor, seventy-one preterm babies had their cerebral and systemic blood flow and oxygen kinetics measured three times in the first 72 hours of life.

The study reconfirmed that gestational age is a strong predictor of early IVH, with the 13 babies whose outcomes were poor being born at a considerably lower gestational age than the other babies in the study. More significantly, the findings enabled the researchers to define new risk thresholds for IVH, which has improved our ability to correctly identify the new-born babies at greatest risk.

“Previous thinking was that IVH was due to low blood supply to the brain, but our data suggests this notion is over-simplistic. It is not merely low blood supply or fluctuating blood supply to the brain but a combination

of low supply and the brain's high requirement for oxygen. In other words, it's metabolic rate,” said Michael.

Michael described this important discovery as a paradigm shift in understanding. With this new knowledge he is confident that in the future, high-risk cases will be more efficiently and effectively identified and offset with preventative therapies.

“We hope this data will rapidly translate into improved clinical care and be used to inform treatment decisions about how to prevent babies going on to develop injury. For example, we are now investigating whether early targeted blood transfusion in babies whose brain's metabolic demand for oxygen exceeds supply might be effective.”

The Neonatal Medicine Research Group has received international attention for this research and their findings were published in the March 2014 edition of the *Journal of Pediatrics*.

Michael and his fellow researchers are continuing to use NIRS to monitor very preterm babies in the first hours of life. They hope their understanding of early IVH will continue to grow and that in future, high-risk babies will face better outcomes.

A new understanding of mastitis

“These findings open the door for a new way of treating and preventing mastitis.”

A/Prof Wendy Ingman

Lactation Mastitis affects around 25% of breastfeeding women inflicting serious flu-like symptoms such as fever and muscle fatigue.

Until recently it was widely accepted that a bacterial infection in the breast caused mastitis and thus doctors prescribed antibiotics to women with the disease. However, when mammary gland biologist, Associate Professor Wendy Ingman began to read the literature on mastitis she questioned the strength of this notion. Wendy recounts how she came to wonder about the origins of mastitis.

“I was giving lectures to 3rd year Health Science students on lactation and mammary gland development. When I started preparing my notes on mastitis I noticed that there was confusing information about causation. Many women have the bacterial infection but do not have mastitis. Similarly, many women who have mastitis do not have the bacterial infection,” she said.

Wendy’s curiosity was stirred and in 2011 she was successful in her application for a Channel 7 Children’s Research Foundation grant with her colleagues. Their hypothesis was a relatively simple one: immune signalling rather than bacterial infection is the primary cause of mastitis.

Her group began testing this theory using a mouse model. All mice were administered a bacterial cell component to induce breast inflammation. However, those mice with a heightened immune signalling pathway (TLR4) developed more aggressive symptoms.

“We showed that the TLR4 immune signalling pathway is really critical in determining the type of immune response and symptoms that an individual woman has when the bacterial infection is present,” Wendy said.

Wendy and her co-researchers suggest that the TLR4 pathway is a significant determinant of mastitis.

“These findings open the door for a new way of treating and preventing mastitis. At the moment, doctors are prescribing antibiotics for the disease but we are beginning to think that a drug that inhibits the inflammation itself might be a more effective treatment,” Wendy said.

More effective treatments will be welcomed by those with mastitis. As well as inflicting new mothers with debilitating symptoms, mastitis often reduces milk supply. Many sufferers have to supplementary feed their babies, which can have implications for the baby’s long-term health.

Wendy and the Breast Biology and Cancer Group are continuing to research the origins of mastitis and hope that they will be able to better define the cause of the disease. With this will come an improved understanding of how to treat lactation mastitis.

This research was published in the May 2014 edition of *Biology of Reproduction*.





“ This phase of the research is about predicting which unborn babies are at risk. ”

Prof Stefan Hiendleder

The impact of the parent's sex on gene expression and fetal growth

Frequently, medical research challenges the veracity of lingering and relatively unsubstantiated ideas.

Recent research has put one such dogma in the firing line: the longstanding notion that a person's genetic make up is essentially a flip-of-a-coin, a battle between mum's and dad's genomes with dominant genes wiping out recessive ones. This research hints at a far more complex and intricate picture where the parental origin of the gene plays a significant role in determining whether the gene is expressed or not.

Professor Stefan Hiendleder, Head of the Epigenetics and Genetics Group, has been studying fetal growth and development, determining whether effects of specific genes differ when they originate from the male or female parent. Using a bovine model, his group have carefully mapped the impact of other variables including the sex of the fetus and the weight of the mother. The culmination of this research is a quite precise

scale of effects that can be used to better predict the likelihood of different genes being expressed and influencing the body structure of the offspring.

This new knowledge is important for understanding mammalian development. However, Stefan is most excited about the human impact of this research, which helps to explain how important metabolic organs such as fetal muscle and bone are involved in fetal programming of susceptibility to postnatal disease such as type-1 diabetes.

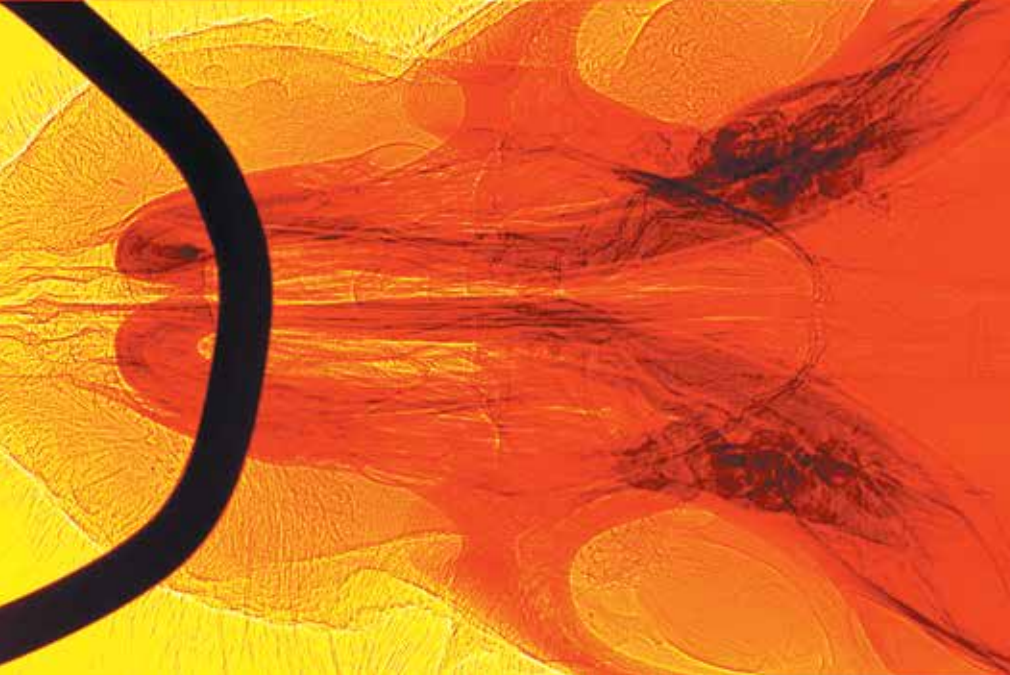
“This phase of the research is about predicting which unborn babies are at risk of being born above or below the optimum weight. We are seeking to identify the genes that play a role in birth weight and defining how likely they are to be expressed and have an impact,” Stefan said.

This new knowledge will lead to better outcomes in pregnancy for both mother and baby.

Stefan, who is an expert in genetics and reproductive biology, is excited by the implications of these findings and is continuing to research gene expression in the bovine fetus model.

“Having the tools and knowledge to predict prenatally the risk to that person's health throughout their life would be an extraordinarily powerful thing,” Stefan said.

With this knowledge, interventions to protect and promote the best outcomes could be developed.



“ This treatment has the potential to ultimately offer a cure for young people with cystic fibrosis. ”

A/Prof David Parsons

Visualising the surface of the lung to treat cystic fibrosis

A decade ago, Associate Professor David Parsons saw images of beetle airway walls generated by X-rays from a synchrotron and was intrigued by their definition and clarity.

David, who is Chief Medical Scientist in the Department of Respiratory and Sleep Medicine at the Women's and Children's Hospital, wondered whether the synchrotron could be used to closely examine the airway surfaces in small mammals, a feat that could have huge implications for lung disease research. David describes that day as a “light-bulb moment”. Since then, David and his colleague Dr Martin Donnelley, together with physicists from Monash University, have been travelling to the Japanese synchrotron bi-annually to develop methods to test cystic fibrosis treatments in living mice. David explains the synchrotron's potential,

“Historically, one of the major challenges in respiratory research has been that what is going on in the lung is very hard to measure. Doctors can do lung function tests, where a patient will blow into a machine and it will offer some information about the overall lung's behaviour, but it gives precious little insight about what is really going on at a cellular level. It's very difficult to get a good understanding about what's happening

within the airway surfaces, where the effects of cystic fibrosis disease are first generated, as it occurs in a tiny but widespread region of airway surface tissue and normal X-rays are not suitable for generating a clear image,” David said.

The synchrotron, which is about the size of a football field, spins electrons around in a gigantic ring and generates extremely bright X-rays. The result is an extraordinarily high-resolution image. Although the machine's radiation is too powerful to use on people, David and Martin have been using it in mice to observe the microscopic changes that would be associated with the pathology of cystic fibrosis, and it's treatment.

Martin said, “We are now able to develop drugs and test them very quickly, and get rapid results. So it's a great developmental tool but it also enables us to test our candidate treatments. We can ask what is the effect of a treatment at that microscopic level? Is the impact achieved quickly or slowly? The synchrotron will lead us to new



understandings about lung physiology and function in cystic fibrosis that were previously beyond our grasp.”

The researchers hope to use the synchrotron to test a gene therapy treatment for cystic fibrosis they have been developing. This treatment has the potential to ultimately offer a cure for young people with cystic fibrosis, especially in early stages of the disease before lungs have been irreversibly damaged.



“We were convinced
macrophages had an
essential role to play in
pregnancy success.”

Dr Alison Care

Essential actions for macrophages in pregnancy

As part of her PhD, Dr Alison Care published illuminating new research identifying the role that macrophages – a specialised subset of immune cells – play in establishing successful pregnancy.

Together with Professor Sarah Robertson and the Reproductive Immunology Group, Alison used a mouse model to demonstrate that the depletion of macrophages in early stages of pregnancy caused miscarriage. However, when macrophages were intravenously replenished to a healthy level before miscarriage occurred, the pregnancy was restored.

“We were convinced macrophages had an essential role to play in pregnancy success,” Alison said.

Alison’s curiosity spurred her to investigate further and she soon discovered a strong correlation between macrophage numbers and progesterone levels. Progesterone plays an essential role in allowing firm embryo implantation and successful pregnancy. She found that when macrophages were depleted, progesterone levels also fell.

When Alison replenished the progesterone it had much the same effect as replenishing the macrophages, restoring the pregnancy.

“Following the macrophage depletion, the dense capillary network in a portion of the ovary that develops in pregnancy known as the corpus luteum was severely disrupted. We then showed that macrophages provide trophic support for this dense capillary network that is essential for the production and distribution of progesterone from the ovary to maintain a healthy pregnancy,” Alison said.

This research builds on the medical understanding of miscarriage and will potentially decrease rates of miscarriage in the future. Alison hopes that it will also help inform the lifestyle and behavioural choices of women who are pregnant or who are trying to become pregnant.

“There are many lifestyle factors that can impact the immune system and therefore affect macrophages. For example, environmental toxins, smoking and obesity affect the way macrophages behave. A better understanding of how these factors affect the immune system may help us to improve pregnancy outcomes and help women who are affected by infertility,” Alison said.

Alison has now graduated from her PhD and is a Postdoctoral Research Fellow at the University of Alberta in Edmonton, Canada where she is working with Professor Sandra Davidge. The findings from her PhD were published in the August 2013 edition of the *Journal of Clinical Investigation*.



“Of course research is done in small steps, but you do aim to ultimately have a real life impact.”

Dr Carmela Ricciardelli

The role of Hyaluronan in chemotherapy resistance of ovarian cancer

Hyaluronan (HA) – a sugar molecule that is a major component of the extracellular matrix – is widely understood to bolster tumour growth as well as drug resistance to cancer.

When Dr Carmela Ricciardelli was investigating the effect of chemotherapy on HA production in ovarian cancer cells, her findings were almost paradoxical: the cancer treatment was triggering a rise in HA levels, a mechanism that might be expected to advance the cancer's aggression.

“We thought that HA levels would probably decrease with chemotherapy and we were interested in understanding why the opposite was the case and the chemotherapy treatment was increasing the production of HA,” Carmela said.

Carmela, a cancer cell biologist at the University of Adelaide and co-leader of the Reproductive Cancer Group, suspected that heightened HA levels were also reducing the impact of chemotherapy. Researchers

tested this hypothesis, treating cancer cells with both HA and common chemotherapy drug, carboplatin.

“We found that the HA made chemotherapy less effective,” Carmela said.

Researchers now know that HA has dual adverse effects, both increasing the expression of ATC-binding cassette transporters and hindering the effectiveness of carboplatin. This combined knowledge suggests new possibilities to increase the potency of ovarian cancer chemotherapy.

“We hope in the future that women with ovarian cancer can be treated with a HA inhibitor to prevent HA levels rising. This might have a two fold effect: blocking the metastatic potential as well as reversing the chemo resistance,” Carmela said.

The next step is to start testing the effectiveness of HA inhibitors on ovarian cancer cells. Carmela is hopeful that this research will one day improve outcomes for women with ovarian cancer, which is the second most common cancer in women and one of the deadliest.

“I want to make a difference for these women. Of course research is done in small steps, but you do aim to ultimately have a real life impact,” she said.

Carmela's research was published in the October 2013 edition of *BioMed Central Cancer*.

Pregnancy in women with kidney disease

“These women need this therapy to keep them alive.”

Dr Shilpa Jesudason

Female patients in the advanced stages of kidney failure are warned about the risk that pregnancy poses to mother and baby.

For these women, becoming pregnant is unlikely, and if pregnancy occurs it can be medically challenging and complicated. So when Dr Shilpa Jesudason, who is a principal researcher in the Transplantation Group, began to assess the ANZDATA registry for these rare high-risk pregnancies, it was unsurprising that there were only 77 recorded cases between 2001-2012.

“I was interested in looking at the outcomes for pregnant women whose kidney disease is at the tip of the iceberg of chronic kidney disease, and who are actually receiving renal replacement therapy, whether it be a full kidney transplant or, in this study, dialysis treatment. These women need this therapy to keep them alive,” Shilpa said.

Research from ANZDATA had already shown that women who received a kidney transplant had significantly better outcomes in pregnancy because of their much-improved health. Shilpa was interested in tracing the outcomes of patients who received chronic dialysis treatment before or during pregnancy.

She recorded a mean 73% live birth rate, which suggests far better odds than suspected.

“This means that if a woman in the advanced stages of kidney failure becomes pregnant, her doctors can advise her that the data suggests a reasonably high likelihood of a living baby at the end of the pregnancy.”

This percentage is higher in women who began chronic dialysis after conception (91%) and lower in those who were receiving therapy at the time of conception (63%).

“My finding suggested that women who fell pregnant when they weren’t on dialysis treatment but started permanent dialysis during the pregnancy were more likely to have live babies. This may be because their kidney failure was not as bad at the time of conception than those already on dialysis. However, once these women reach twenty weeks gestation, there was little difference in the outcome between the two groups. Most pregnancy losses were occurring in the early stages,” Shilpa said.

These findings suggest that those women who are healthier at the time of conception and begin dialysis during the pregnancy are likely to have a live baby. However, Shilpa stressed that these babies are still born prematurely and have a low birth weight, something that might have serious implications for their long-term health and development.

The next phase of this research is to analyse these pregnancies more closely and to clearly define the variables that cause some women to have better outcomes than others.

“My finding suggested that women who fell pregnant when they weren’t on dialysis treatment but started permanent dialysis during the pregnancy were more likely to have live babies.”





Commercial development

Advancement in reproductive and paediatric health relies on new technologies, commercial innovations and successful partnerships. Innovative research discoveries made in the Robinson Research Institute are transforming medical practice and the health of our community.

In 2013 the Institute generated over \$1 million in contract research and consulting income through a wide variety of industry partners

Clinical trials

Sponsored clinical trials to evaluate new vaccines and new IVF products are underway with a number of companies including Merck Serono Australia, Medpace Australia and Merck Sharp & Dohme (Australia) Pty Ltd and Merck and Bayer.

EmbryoGen®

In April 2013 the first baby was born in Australia using EmbryoGen®, a treatment product for miscarriage containing cytokine Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF).

Developed in collaboration with Origio A/S, EmbryoGen® offers a novel treatment option for women undergoing in vitro fertilisation (IVF) after a history of one or more miscarriages. The science behind the technology is led by Professor Sarah Robertson, who has spent more than 20 years working on cytokine regulation of embryo development. The key to its success is the technology's ability to closely mimic the natural environment of the uterus and support early growth and firm implantation. Embryogen is now available in more than 50 countries internationally and Origio is negotiating with the Therapeutic Goods Association to make it more widely available in Australia.

New trials to evaluate a blastocyst culture medium containing GM-CSF are planned in partnership with Fertility SA and the Institute for 2015.

IVF Vet Solutions

The IVF Vet Solutions business unit, led by Associate Professor Jeremy Thompson, provides services to the human and veterinary IVF market. This includes the Mouse Embryo Assay (MEA), a quality assurance test for media and other products used in IVF. A variety of national and international companies and IVF labs utilise this service.

The unit has also developed a suite of bovine IVF media, with significant sales of media to Australian Reproductive Technologies PTY LTD and OVASEM PTY LTD. The media is being exported to a number of countries including Canada, South Africa and USA.

Expert Panel to the NHMRC

The Australian Research Centre for Health of Women and Babies (ARCH) team, led by Philippa Middleton, was re-appointed to the NHMRC panel of providers with expertise relevant to the development and presentation of evidence based health advice. ARCH continues to develop the national evidence-based antenatal care guidelines and also provide expert advice to Cancer Australia in relation to the grading of clinical practice recommendations.

Production and supply of antibodies

Professor David Kennaway has a commercial partnership with Buhlmann Laboratories involving the supply and use of antibodies to detect the hormone melatonin. The antibodies are incorporated into kits sold by Buhlmann to measure melatonin for laboratory and clinical applications.

Biomarker translation

As part of a biomarker discovery program jointly funded by the CRC for Biomarker translation and the NHMRC, a novel biomarker of immune cell subsets PI16, also named CD364, has been developed by Associate Professor Simon Barry.

Beckton Dickinson now licenses this biomarker for sale on the international market. The antibody is being tested for diagnostic utility in a number of diseases including type-1 diabetes, IBD and infertility, and is a new tool to advance research into regulatory T lymphocytes in laboratories around the world.



Collaboration with Cook Medical

Institute leaders enjoy a strong relationship with Cook Medical LLC - a large privately owned medical device company based in Bloomington Indiana, USA. Cook make over 30,000 medical and surgical products, and their Women's Health Division is a global producer of IVF products.

For the past 10+ years, Cook have partnered on grants, engaged Associate Professor Jeremy Thompson and Dr Robert Gilchrist as consultants, and supported many research projects which focus on development of assisted reproductive technologies.

Cook have supported patent filings related to these technologies, and also resourced the Robinson Research Institute to fund the China exchange grant. Cook is a commercial partner in the Premiers Science Research Fund and Australian Research Council Linkage Grants related to the STARR lab, which is a joint project between the Robinson Research Institute and the Institute for Photonics and Advanced Sensing (IPAS).

New patents

Continuing a strong culture of commercial innovation, Robinson Research Institute members filed several new patent applications in 2013 in the areas of mastitis technology, swallowing disorders and biomarkers for ovarian cancer.

Robinson Research Foundation



A message from the Chair

The work that is undertaken at the Robinson Research Institute never ceases to amaze me. As Chair of the Foundation I am fortunate to meet some of the Institute's world-leading researchers and learn about their important work. Their passion and dedication to addressing major health issues in our community is truly inspiring. It is for this reason we must continue to focus on raising awareness of this vital research work and the important place it has in our society.

The breadth and depth of research discoveries that emerge through the Robinson Research Institute need to be widely recognised among the general community – and this is an ongoing quest, where we can make a real difference.

We seek to educate the community about the myriad of health risks associated with fertility, pregnancy, the health of babies, children and adolescents, and the impact of health across generations.

We need to raise much-needed funds to support new and ongoing research to ensure our discoveries can continue and that they can be transformed into clinical care and policy for the health of all children and families, across generations and global communities.

I would like to extend my personal thanks to the Robinson Research Foundation for their support and commitment to the Foundation and the Institute throughout 2013. I also take this opportunity on behalf of the Committee to extend our sincere thanks to all past members of the Foundation for their support and commitment. To members past and present, their contribution since the Foundation commenced is greatly appreciated.

Our supporters and donors are essential to helping us achieve our goals. On behalf of the Foundation and members of the Robinson Research Institute, thank you for your ongoing support.

During 2013 the Foundation has taken the opportunity to review its strategy for fundraising. A fresh look at working in partnership with the University's Engagement Branch and work behind the scenes to develop unique opportunities are being explored. We look forward to putting the outcomes into practice as we embed the new strategy for the future.

Neil Howells

Chair Robinson Research Foundation



Prof Andrew Zannettino, Prof Ray Rodgers, A/Prof Helen Marshall and Dr Alexia Pena

Engagement

In 2013 we participated in a series of initiatives that enabled us to engage with the community to raise awareness of the Institute's research:

Excellence In Research Dinner - Macquarie Private Wealth

The Excellence in Research Seminar Series is presented by Macquarie Private Wealth, and provides insight into significant research within each of the University of Adelaide's five research institutes. The Robinson Research Institute participated in the 2013 series - with Professor Sarah Robertson sharing the latest research into preterm birth.

15 million babies are born preterm every year - 1 in 10 - and the rate is increasing. Globally, preterm birth is the leading cause of newborn death and the second cause of death in children under 5 years of age. Of those babies who survive, many suffer serious short and long-term health problems including greater risk of cerebral palsy, blindness, deafness, learning and developmental problems, and adult onset disease. The Robinson Research Institute has identified preterm birth as a key research priority and members across the Institute are leading the way in uncovering the causes and prevention of preterm birth.

Through the Excellence in Research Dinner held on 18 September, funds raised were generously matched by Macquarie Private Wealth and will be directed towards ongoing research efforts into preterm birth. We thank our generous supporters for their donations. We also thank Macquarie Private Wealth

for not only hosting the event but also their generosity in matching the donations pledged and raised on this occasion.

The Robinson Research Institute is committed to continuing this important research and will support the team in its fundraising efforts.

ASMF Clipsal Ladies Day Luncheon

The Robinson Research Institute were delighted to be a recipient organisation at the 2013 ASMF Clipsal Ladies Day Luncheon. Held in February, the annual event delivered by The Advertiser Sunday Mail Foundation continues to grow each year with record numbers of attendees. Funds raised on the day were directed towards furthering our research in the fields of fertility, pregnancy and child health. The Robinson Research Institute sincerely thanks Lasertech Clinic & Luxury Spa for their generation donation and The Advertiser Sunday Mail Foundation.

Unique fundraising initiatives that served to engage with the community and raise funds included:

- > Giving Tuesday: Tuesday 6 December 2013 was chosen to be a day of giving around the globe. The Robinson Research Institute reached out to its generous supporters and raised funds to support preterm birth research.
- > Uncorked: Hosted by the National Wine Centre, Uncorked is a fortnightly Friday event showcasing South Australian wineries. In March 2013, The Robinson Research Institute and Tapestry Wines were the partnering organisations and part proceeds of sales on the night were donated to the Institute to support preterm birth research.
- > Adelaide Entertainment Book: In 2013 the Robinson Research Institute raised funds for preterm birth research through sales of the Adelaide Entertainment Book - selling close to 100 books.

Robinson Research Foundation Committee 2013

Mr Neil Howells (Chair)

Ms Joanna Close

Mr Stephen Couche

Mr Paul Griffin

Mr Alf Ianniello

Emeritus Professor Colin Matthews

Mr Ian Nightingale

Dr Dyann Smith

The Robinson Research Institute through the Foundation supports the life-giving research of the Institute. Our aim is to:

- > Raise 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
- > Raise public awareness of the clinical and policy benefits of the work of the Robinson Research Institute in order to enhance the uptake of research findings from the Institute by the community

To achieve this, the Robinson Research Institute works closely with its Foundation Committee, who generously offer their time, support and expertise.

Peter Couche Foundation



In reality, this has entailed supporting the work being carried out by Professor Simon Koblar, who leads the Stem Cell for Stroke research group at the Robinson Research Institute. This group is the only one of its kind in the country. At present, and having raised more than \$600,000 in funds from both corporate sponsors and the general public, the group's focus is to fund the first (anywhere in the world) human dental pulp stem cell trial.

A target has been set for mid 2016 for a Human Phase 1 clinical trial that will involve the injection of neural stem cells from stroke patient's teeth into their own stroke-affected brain. This trial would be the first of its kind undertaken in the southern hemisphere and one of only a few ever undertaken in the world.

The principal function of the Peter Couche Foundation is to spread awareness of stroke and to raise vitally needed funds for research into brain repair following a stroke.

Peter Couche was a successful stockbroker and father of three when he suffered a stroke at age 42 (over 20 years ago). Peter's stroke left him a quadriplegic with 'Locked-in Syndrome' - he cannot speak and has little muscle control but has an active and alert brain, and is determined to make a difference to those who have suffered a stroke.

In association with the University of Adelaide, Peter established the Peter Couche Foundation in 2009 to increase awareness of stroke and raise vital funds to support the Robinson Research Institute's Stroke Research Program. Led by renowned stroke physician and researcher Professor Simon Koblar, the team is currently researching the use of stem cells from the adult human tooth, called dental pulp stem cells (DPSCs), as a potential therapy for brain repair in stroke victims. Research to date has indicated that DPSCs have an ability to produce neurons and make a range of growth factors that are likely to help repair the brain.

Since launching in 2009, the Foundation has raised more than \$600,000, with \$140,186 being raised in 2013 alone to progress this important research. Major research developments and fundraising initiatives are

outlined below; including the Foundation's involvement in the Adtrans Golf Day and the annual Peter Couche Foundation Wine Dinner.

From all of our researchers and the team at the Peter Couche Foundation we would like to thank our generous donors and supporters. Through your ongoing collaboration we have significantly progressed this important research agenda, which could aid stroke sufferers in the near future.

Research Developments

The Peter Couche Foundation has achieved a great deal in raising the profile of this type of therapy for stroke – funding the first research project to show how human adult stem cell treatment from the tooth improves brain function.

In 2013, the group continued their neuroplasticity research, by administering DPSC intravenously rather than via an injection into the brain.

In 2013, Simon's group finalised a pre-clinical study investigating how best to deliver DPSC and if improvement is achieved when DPSC are administered days after stroke.

2013 Activities

Don't Speak, silence for stroke

What would your life be like if you couldn't speak? Couldn't express an opinion, ask a question or tell your children you love them?

This is the question we ask our supporters who participate in the Don't Speak, silence for stroke fundraising campaign. Peter Couche and thousands of stroke sufferers across Australia know exactly how this feels.

Approximately 60,000 people suffer a stroke in Australia every year, which can result in loss of memory, speech or movement. Don't Speak aims to raise awareness of the impact that stroke can have on an individual, their family and friends by asking participant to be silent for at least an hour.

In 2013, 27 participants pledged to be silent for at least one hour and sought sponsorship to support the cause. Together they successfully raised over \$35,000 with Andrew Brown from Adrian Brien Automotive being the top fundraiser for the second year running.

Thank you to ambassadors Tom Harley, Kate Collins, Tracy Gibb and His Excellency Rear Admiral Kevin Scarce AC CSC RANR - The Governor of South Australia, for their help with raising awareness and their ongoing support.

Stem Cell therapy public seminar

In August, Professor Simon Koblar presented a free public forum on the topic Stem Cell Therapy for Neurological Disease.

In his seminar he discussed stem cell biology and its potential use in therapy to treat not only stroke, but a range of neurological diseases including multiple sclerosis, parkinson disease, spinal cord injury and motor neuron disease.

This seminar was well received with more than 150 attendees and helped to provide hope for those living with a disability. Simon also explained why its time to plan for a clinical trial in Adelaide to treat local stroke survivors who have a disability.

Adtrans Golf Day

In November, Adtrans Automotive Group supported the Peter Couche Foundation for the third year in a row through its annual Charity Golf Day.

The day was a record success for Adtrans with over \$25,000 being donated to the Peter Couche Foundation.

Thank you again to Adtrans for your hard work, enthusiasm and support.



Peter Couche Foundation Wine Dinner

In October 2013, over 150 supporters attended the Peter Couche Foundation annual Wine Dinner and through their generosity raised over \$45,000 for stem cell for stroke research.

Held at the National Wine Centre in Adelaide, guests were treated to a three-course meal matched with premium wines, heard from leaders in the wine industry, and enjoyed entertainment from Acoustic Juice who generously donated their time.

In addition guests were lucky to hear from Peter Couche Foundation ambassador Tom Harley who provided commentary on the AFL season as well as explained his involvement with the Peter Couche Foundation. Kate Collins was generous to donate her time to MC the evening.

Thank you to all our sponsors and auction contributors, your valued support made the event a success. In particular we would like to recognise the generosity of Orlando Wines, Holco and the National Wine Centre.

Peter Couche Foundation Committee

Mr Stephen Couche (Chair)

Mr Dom Cosentino

Mr Peter Couche

Mrs Simona Couche

Mr Colin Dunsford

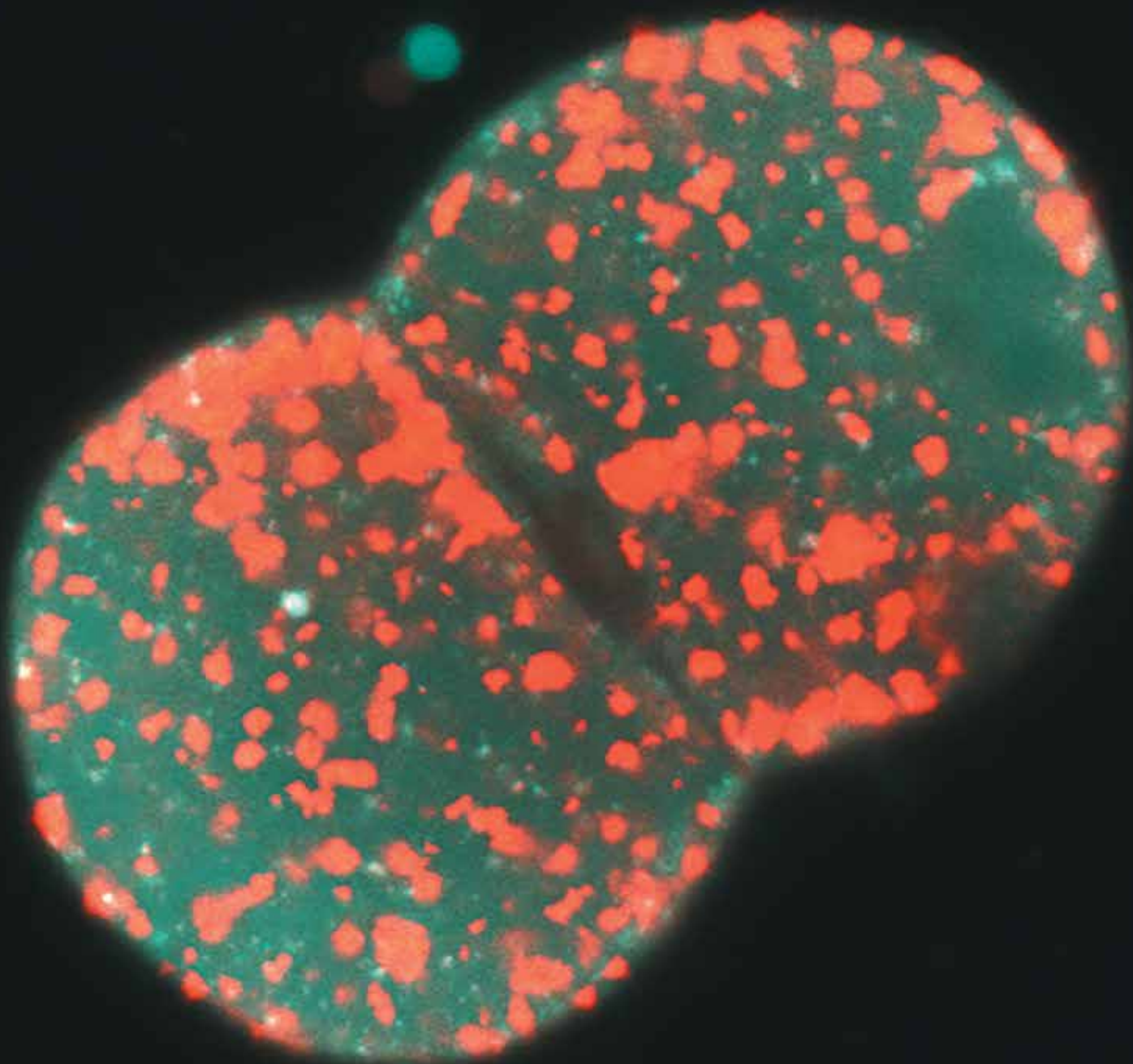
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Ms Alissa Nightingale

Mr Stephen Officer

Mr Mick Scammell

Ms Lisa Taplin



Metabolic analysis of 2-cell mouse embryo following exposure to epigenetic modifying drug

Research capacity building

To achieve our goal of delivering world-class advances in knowledge of human reproduction, pregnancy and child health, the Robinson Research Institute is investing in people, networks and facilities.

To build skills, experience and leadership in our current and future researchers, the Institute delivers a number of programs and scholarships.

Exchange

The Exchange Program provides funding support for members to either host senior researchers visiting the Institute, or for members to travel to host institutions.

The program aims to build relationships with overseas and interstate collaborators

for the benefit of the Institute and its members, to grow current and potential future collaborations with strategic interstate and overseas partners, to expand national and international awareness of research at the Institute, and to build research capability and facilitate access to international funding, databases and expertise.

In 2013, 12 visitations were supported, building links with research groups from the UK, USA, Canada and China. Five international researchers visited the Institute and 7 members travelled overseas.

Networking Forum

The Networking Forum Program provides funding support for networking activities, workshops and meetings. It aims to encourage and extend collaboration, share knowledge and explore new research ideas across the Institute. It seeks to create the potential for new external collaborations with interstate and overseas partners.

Professional Development

The Robinson Research Institute is committed to investing in ongoing professional development for its researchers. In 2013, professional development funding was used to send 5 Research Leaders to a one-day media-training course run by "Science in Public". The course was practically oriented and engaged journalists from Channel 10 News, The Australian newspaper and MIX radio. Participants appreciated the practicality of the course, the professional insights from journalists, the small group, 1-on-1 practice, and the feedback provided.

“ Well organised, clear and achievable goals, challenging and at times uncomfortable tasks, critiqued performance, and well-modelled communication.”

Dr Warwick Teague, 2013 participant

Visitors to Robinson Research Institute

Dr John Bromfield Dept of Obstetrics and Gynecology and Women's Health, University of Missouri, USA

RRI Host: Prof Sarah Robertson

Prof Richard Alexander Anderson MRC Centre for Reproductive Health, University of Edinburgh, UK

RRI Host: Prof Raymond Rodgers

Prof William Elbert Rainey Dept of Molecular & Integrative Physiology, University of Michigan, USA

RRI Host: Prof Raymond Rodgers

Ms Sheryl Rifas Department of Population Medicine, Harvard Pilgrim Health Care Institute, Boston USA

RRI Host: Prof Jodie Dodd

Dr Nick Lu Dept of Medicine, Northwestern University, Chicago USA

RRI Host: A/Prof Vicki Clifton

Hosts to RRI Researchers

Prof David Olson Women's and Children's Health Research Institute, University of Alberta, Canada

RRI Visitor: Prof Sarah Robertson

Prof Richard Stouffer Oregon National Primate Research Center, Oregon Health & Science University, USA

RRI Visitor: Dr Rebecca Robker

Prof Debbie Lawlor MRC Integrative Epidemiology Unit, University of Bristol, UK

RRI Visitors: Prof Julie Owens and Dr Julia Pitcher

Prof Ji Wu Bio-X Institutes, Shanghai Jiao Tong University, China

RRI Visitor: Dr Katja Hummitzsch

Prof Siladitya Bhattacharya Institute of Applied Health Sciences, University of Aberdeen, UK

RRI Visitor: Prof Michael Davies

Dr James Turner Stem Cell Biology and Developmental Genetics, MRC National Institute for Medical Research, London, UK

RRI Visitor: Dr Tasman Daish



Career Development Fellowship

The Career Development Fellowship funds the salary of an Institute “Emerging Star” early career researcher for one year. This supports an individual to develop a competitive application for a NHMRC Career Development Fellowship, or similar nationally competitive fellowship scheme.

The 2014 Fellowship (awarded 2013) was split between Dr Hannah Brown and Dr Tamara Varcoe.

Investment for Success

The Investment for Success Program supports competitive NHMRC project grant applications that were highly ranked but unfunded in the 2013 round, so they may be developed into more highly competitive applications for resubmission in 2014. The funding is utilised for activities to sustain research progress while preparing applications for future success.

2013 Recipients:

- > Dr Carmela Ricciardelli
- > A/Prof Jeremy Thompson
- > A/Prof Helen Marshall
- > A/Prof Vicki Clifton
- > A/Prof Simon Barry
- > Dr Louise Hull
- > Prof Tony Ferrante
- > Dr Nicki Hodyl
- > A/Prof David Parsons

Mentoring Program

The Mentoring Program was established as an important step to career orientation and personal development for members of the Institute. Mentors – typically senior researchers or research leaders – volunteer their time to mentor early-career researchers and offer support in career and skills development. Mentees are matched with Mentors according to their research interests and specific requirements. Now in its third year, the program has proven to be of great benefit to both Mentees and Mentors.

The Mentoring Program aims to:

- > Develop and support researchers in their respective career stages
- > Increase the skills of members
- > Develop an awareness of the importance that networking can have on future career opportunities, and commence appropriate networking activities
- > Facilitate relationship building amongst members of the Institute, as a step towards future collaboration
- > Provide empowerment opportunities where members can engage in leadership roles
- > Enhance researcher credentials for CVs, grants and other applications
- > Help members to gain an understanding of the broader Institute activities and initiatives, how they fit into the Institute and the value and potential of the work they do from a broader perspective

Training the next generation

The Robinson Research Institute is committed to training the next generation of researchers through Honours and Higher Degree by Research programs. In 2013 the Institute had more than 30 Honours students and more than 130 PhD students.

Jeffrey Robinson Honours Scholarship

In 2013, the Robinson Research Institute offered the Jeffrey Robinson Honours scholarship to an outstanding Honours student, Zuleeza Ahmad.

During her undergraduate study at the University of Adelaide, Zuleeza developed an interest in investigating the relationship between placental abnormalities and adult metabolic outcomes.

Her honours project was titled: *The Effects of Placental Growth Restriction on Plasticity of Insulin Secretion in Response to Hyperglycemic Challenge in Adult Sheep*. This looked at how adaptive changes or plasticity of insulin secretion is altered following a chronic mild hyperglycaemia in growth restricted adult sheep.

As an international student, Zuleeza was particularly grateful for her scholarship as it assisted in funding the cost of a temporary student visa and other essential items to continue her studies.

The scholarship enabled Zuleeza to pursue her research interest and she continually finds it to be a rewarding career choice:

“No matter how little or how big the progress I make, I know I could potentially be on my way to make an impact towards a better quality of life.”

“Despite popular belief that research is repetitive and dull, I find that no two days are alike in research world. Every day poses a new challenge and a new revelation of how my project may end up and for that very reason, I believe research is fun and exciting.”

Zuleeza has now completed her Honours project under the supervision of Dr Kathy Gatford, Dr Tina Bianco Miotto and Prof Julie Owens and is currently pursuing a PhD in molecular sciences.



Travel grants

The Travel Grant Program is a joint initiative between the Robinson Research Institute and the School of Paediatrics and Reproductive Health. It provides members with the opportunity to present and share their research findings at national and international conferences and meetings. By attending such events, researchers are able to network with interstate and overseas researchers, expand their CVs and develop relationships for future collaborations. In 2013, 50 research staff and HDR students were awarded travel grants.

Member	Supervisor	Abstract
American Anthropological Association (Chicago, USA)		
Tanya Zivkovic		Short horizons and obesity futures
American Society for Reproductive Medicine (Massachusetts, USA)		
Miaoxin (Victor) Chen	Leonie Heilbronn	1. Decreased insulin sensitivity in young adults born through in vitro fertilisation (ivf) and higher systolic blood pressure following high fat overfeeding 2. Distinct adult metabolic consequences following ovarian stimulation versus in vitro culture of mouse embryos
Australasian Brain Stimulation Meeting 2013 (Melbourne, Australia)		
Ann-Maree Vallence	Michael Ridding	Functional connectivity in the ageing motor system
Luke Schneider	Julia Pitcher	Cognitive outcomes after preterm birth
Mitchell Goldsworthy	Michael Ridding	De-depression and consolidation of neuroplastic changes in the human motor cortex
Australasian Cystic Fibrosis Conference (Auckland, NZ)		
Martin Donnelley	David Parsons	Advances in airway surface imaging for Cystic Fibrosis: Extended monitoring of individual particle mucociliary clearance
Patricia Cmielewski	David Parsons	Improved Survival by Airway Lentiviral CFTR Gene Transfer in a Cystic Fibrosis Mouse Model
Cochrane Colloquium (Quebec, Canada)		
Emily Bain	Philippa Middleton	The antenatal magnesium sulphate for fetal neuroprotection research cycle: beyond the meta analysis
Developmental Origins of Health and Disease (Singapore)		
Consuelo Amor Estrella	Stefan Hiendleder	Novel paternal genome effects on placental and fetal phenotype at midgestation
Himawan Harryanto	Julie Owens	Placental restriction altered insulin actions and increased microRNA expression in insulin sensitive tissues of adult offspring in the rat
Hong Liu	Julie Owens	Can neonatal extendin-4 prevent obesity after IUGR
Luke Schneider	Julia Pitcher	Early life influences on cortical excitability and cognitive outcomes in adolescents
Nicole McPherson	Michelle Lane	Paternal lifestyle interventions in obese males restores early embryo development and fetal weights, improving the metabolic health and adiposity status in subsequent female offspring
Tod Fullston	Michelle Lane	An animal model of paternal obesity programs metabolic disturbances in two generations of mice and alters the transcriptional profile of founder testis and sperm microTNA content
Early Nutrition The Power of Programming (Munich, Germany)		
Rosalie Grivell		The effect of antenatal dietary and lifestyle advice on fetal growth in women who are overweight or obese: findings from the LIMIT randomised trial
Endocrine Society of Australia & Society for Reproductive Biology (Sydney, Australia)		
Amy Wooldridge	Julie Owens	Does late pregnancy methyl donor supplementation reverse effects of placental restriction on immune function in sheep?
Bihong Zhang	Sarah Robertson	Repeated exposure to male seminal fluid expands uterine regulatory T cell and antigen presenting cell populations during early pregnancy in mice.
Dulama Richani	Rob Gilchrist	Effect of EGF-like peptides on the metabolism of in vitro matured oocytes and their associated cumulus cells
Hanan Hamimi Binti Wahid	Sarah Robertson	Toll-like receptor signalling in inflammation pathways to preterm delivery
Hannah Brown	Jeremy Thompson	Haemoglobin: A gas transport molecule lost during oocyte in vitro maturation (IVM)
Hong Liu	Julie Owens	Can neonatal extendin-4 prevent obesity after IUGR?"
Jacky Sudiman	Rob Gilchrist	The pro-mature form of bone morphogenetic protein 15 (BMP15) in oocyte maturation medium improves subsequent bovine embryo development
Jonathan McGuane	Louise Hull	TGF beta 1 downregulates the production of bone-related factors in human endometrial stromal cells
Kathryn Gatford	Julie Owens	Placental restriction impairs plasticity of insulin secretion
Katja Hummitzsch	Ray Rodgers	Is focimatrix required for the luteinisation of follicular granulosa cells
Linda Wu	Rebecca Robker	By reversing endoplasmic reticulum stress can improve poor oocyte quality found in a novel obese mouse model- Blobby Mouse
Lisa Akison	Darryl Russell	Nuclear progesterone receptor-regulated gene networks in the oviduct: potential mediators of progesterone action on oviductal transport
Melanie McDowall	Jeremy Thompson	Addition of an ER-stress inhibitor overcomes the compromised development of cow COCs matured in vitro with elevated fatty acids
Miaoxin (Victor) Chen	Leonie Heilbronn	Metabolic phenotyping of young adults and mice conceived by In Vivo Fertilisation
Michael Boden	David Kennaway	Chronic phase shifting in rats disrupts rhythmic gene expression, impairs glucose tolerance, insulin secretion and sensitivity
Peck Yin (Loretta) Chin	Sarah Robertson	Low dose LPS insult during pre-implantation period programs fetal development
Sam Buckberry	Claire Roberts	Non-coding RNAs as key regulators of placental development

Member	Supervisor	Abstract
Endocrine Society of Australia & Society for Reproductive Biology (Sydney, Australia)		
Siew Leng Wong	Rebecca Robker	Exposure to high glucose and lipid impair oocyte developmental competence in association with ER-stress and O-GlcNAcylation
Tamara Varcoe	David Kennaway	Characterisation of the maternal response to shiftwork: implications for fetal metabolic programming
Tina Bianco-Miotto	Claire Roberts	A maternal high fat diet increases the incidence of prostate cancer in male offspring using a transgenic mouse model
Tod Fullston	Michelle Lane	Paternal obesity initiates metabolic disturbances in two generations of mice and concomitantly alters the transcriptional profile of testis and sperm microRNA content
Xuan (Sally) Sun	Wendy Ingman	Impaired TGFB signalling in macrophages perturbs mammary gland development
European Molecular Biology Laboratory Australia (Melbourne, Australia)		
Natalie Aboustate	Nicki Hodyl	Workshop attendance
European Society of Pediatric Endocrinology (Milan, Italy)		
Jemma Anderson	Jenny Couper	Time lying down and energy expenditure are important determinants of vascular health in T1D children.
Fertility Society of Australia (Sydney, Australia)		
Helana Shehadeh	Michelle Lane	Paternal obesity impairs the reproductive health and ovarian molecular profile of their female offspring
Fragile X (Barossa Valley, South Australia)		
Kristie Lee	Cheryl Shoubridge	Investigating the molecular pathogenicity of ARX polyalanine expansion mutations in X-linked intellectual disability
Tessa Mattiske	Cheryl Shoubridge	Polyalanine tract expansions impact on ARX and its interaction with UBQLN4: Aggregation vs. Degradation?
Gordon Research Conference in Mammary Gland Biology (Stowe Vermont, USA)		
Siti Noor Din	Wendy Ingman	Effect of C1q null mutation on mammary gland tumourigenesis
International Congress of Immunology (Milan, Italy)		
Kanchana Usuwanthim	Tony Ferrante	Regulation of complement receptor immunoglobulin (CRIg) expression in human macrophages by protein kinase cx
International Federation of Placenta Associations (Whistler, Canada)		
Astrud Tuck	Vicki Clifton	Identification of candidate genes in human placenta involved in the development of childhood allergy
International Pancreas and Islet Transplant Association (California, USA)		
Mariea Bosco	Toby Coates	Early changes in zinc and zinc transporters in a type-2 diabetes db/db mice pancreatic islets
International Union of Nutritional Science (Grenada, Spain)		
Wing Hong (Vincent) Chu	Julie Owens	Hepatic Transcriptional Consequences for Young Adult Female Progeny Following Folic Acid Exposure in Gestation
Mammalian Embryo Genomics (Quebec, Canada)		
Hannah Brown	Jeremy Thompson	Hyperglycaemia: a new player in oocyte epigenetics
North American Vascular Biology Organisation (Massachusetts, USA)		
Kate Parham	Claudine Bonder	Endothelial progenitor cell differentiation: A role for Peroxisome proliferator-activated receptor γ
Paediatric Rheumatology European Society (Ljubljana, Slovenia)		
Christina Boros		Fatty acid profiling: potential new biomarkers in juvenile idiopathic arthritis
Pharmacoepidemiology & Therapeutic Risk Management (Montreal, Canada)		
Luke Grzeskowiak	Vicki Clifton	1. Antidepressant use in late gestation and breastfeeding rates at discharge from hospital 2. Prenatal antidepressant exposure and child behavioural outcomes at 7 years of age 3. Use of Serotonin Reuptake inhibitors in late gestation and lactation difficulties 4. Maternal smoking in early pregnancy increases risk of childhood overweight
Reproductive Immunology (Shanghai, China)		
John Schjenken	Sarah Robertson	Sperm Mediated Signaling in the Female Reproductive Tract of the Mouse
Society For Neuroscience (San Diego, USA)		
Lachlan Jolly	Jozef Gecz	USP9x is a Novel X-Linked Intellectual Disability Gene that regulates Neuronal Migration and Axon Growth
Thomas Klaric	Simon Koblar	Npas4 is upregulated in the corticolimbic system of the rodent brain following focal cortical ischaemia
Society for the Study of Reproduction (Montreal, Canada)		
Hannah Brown	Jeremy Thompson	A gas transport molecule lost during oocyte in vitro maturation (IVM)
John Schjenken	Sarah Robertson	Induction of endogenous MiR223 expression by sperm in the female reproductive tract following mating in mice
Lisa Akison	Darryl Russell	Progesterone Receptor-Regulated Gene Networks in the Oviduct: Potential Mediators of Oocyte and Embryo Transport
Society of Gynecologic Investigation (Orlando, USA)		
Mohammad Zahied Johan	Louise Hull	Activation status of macrophages in lesions from a MacGreen/ SCID mouse model of endometriosis
World Congress of Endometriosis (Sao Paulo, Brazil)		
Jonathan McGuane	Louise Hull	Seminal plasma stimulates endometrial cytokine production and promotes endometriosis-like lesion development
Zhao Wang	Louise Hull	Plasma microRNAs: a promising diagnostic biomarker for endometriosis

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Haysom Sally	Kelly Vivienne	McEgan Chris	Peterson Daniel	Sellars Patsy	Waddell Neadree
Heard John	Kennedy Chris	McGillick Erin	Phil Hoffman Travel	Sharp Michael	Wagenfeller Karl
Heidiwho?	Khan Marisa	McKinnon Brett	Philp Kimberly	Shaw and Smith	Wakefield Press
Henderson William	King Y	McLachlan A	Pierce Denis	Sheldrick Tom	Walsh Brian
Henderson Ambrose	King Cherise	McLean Tamsin	Piotrowska Dominika	Sheldrick Sue	Walsh Richard
Henderson-Wilson Chad	King Dianne	McLennan Wendy	Pirrello Vince	Silvio Amanda	Walsh David
Henry Pip	Kingston Peter	McLeod David	Plummer Phil	Simmonds Fiona	Walsh Sarah
Hentley Farm	Kitto Marion	McPhee Katharine	Pollock Bronwyn	Sinicropi Assunta	Wark James
Herriman Sandra	Kitto Beth	Megins Catherine	Pomfret Julie	Smart Bev	Warren Daryl
Hicks Les	Kitto Damien	Michelmores Chris	Powell Kris	Smerdon Chris	Waterhouse Tim
Hill Alex	Klaric Thomas	Mikulcic Angelika	Prass Gunter	Smith Geoff	Watts Heidi
Hill Damien	Klein Lindsay	Miller Peter	Pratt Coralie	Smith Craig	Wei Steven
Hillier Susan	Kleinig Tim	Miller Lesley	Prosser Lis	Smith Adam	Weinberg Tracy
Hoey Wade	Klingberg David	Milutinovic Mia	Prowse Sue	Smoker Luke	Whelan John
Hogan Neil	Klobas Marko	Mitchell Carolyn	Purdie Grant	Sparrow Richard	White Peter
Hogg Michelle	Knagge Greg	Mitchell Karen	Pynor Phil	Speakman Philip	White Alyssa
Hopkins Andrew	Koblar Simon	Mladenovic Aleks	R.M. Williams	Spencer Kristine	Whitford Ashleigh
Hornibrook Craig	Koerner Jim	Moet Hennessy	Raffa Rob	Stark Kathy	Whitford Brittany
Horton Tim	Kontic Rachel	Montgomerie Heather	Rains Ray	State Opera SA	Whittaker Jillian
Hoskin Zana	Krahe Ashleigh	Moran Jessica	Rana Maya	State Theatre	Wilkins Francis
Houlihan Jane	Kranixfeld Sonia	Morris Tessa	Ranasinghe Pushpa	Steel Jodie	Williams Mark
Howden Rob	Krawczyk Gene	Morton Phil	Rawson John	Stephen Couche	Wilsey Ashley
Howe Rosemary	Krawczyk Jason	Munn Alicia	Raywood Michael	Stephens Courtney	Wilson Sharon
Howell Sam	Krawczyk Jenna	Murphy Grace	Redman Julie	Stephenson Russell	Wilson Danni
Howells Neil	Krcmarova Jana	Murphy Lisa	Reynolds Wendy	Steven Annie	Winderlich Josh
Hugh Hamilton	Krueger Susan	Muscat Juliana	Reynolds Burton	Stirling Greg	Winnall Chris
Hughes Tim	Kuang Justin	Myler Bernadette	Richardson Matt	Stobbe Rob	Winter Nigel
Hughes Evan	Kupke Tim	Mynott Jenna	Richards Wayne	Street Celia	Woods David
Hughes PR	Ladd Helen	National Wine Centre	Richardson Anika	Stuart Toby	Wright Gael
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Hulshof Frank	Laidlaw Sonia	Neldner Simon	Richardson Matt	Sweet Ann-Marie	Yeend Luke
Humphrys Jim	Lane Narelle	Neville Sally	Ridge David	Sweet Karen	Yeend Susan
Hunt Bob	Lange Brian	Newnham Erina	Roberts Esther	Swift Shaun	Yeend Emma
Hunt Susan	Larkins Conor	Ngo Tri	Roberts John	Synnottt Barry	Yeoh Neil
Hurn Ben	Leabon Aimee	Nicolo Paul	Roberts Teya	Tam Mia	Young Stephen
Iacovino Mike	Lecat Isabelle	Nightingale Dianne	Robertson Sarah	Tan Aaron	Zhang Aileen
Irving Kate	Leedwell Property	Nightingale David	Robinson Tanja	Tanner Rosemary	Zhong Athena
Irving John	Li Joule	Nightingale Kerrie	Robinson Teena	Tao Tracy	Zwarycz Josie
Ivancic Marino	Lienert Lorraine	Nomchong Anthorr	Rockford Wines	Teaman Brian	
Jackson Matilda	Lim David	Nor Azman	Rodriguez Karen		

Member list

This acknowledges the 2013 membership of the Robinson Research Institute; we have aimed to capture as comprehensive a list as possible and any omissions are unintentional. We would like to recognise the contribution of all members, with a special mention to the School of Paediatrics and Reproductive Health's administration team led by Michael Guerin, School Manager.

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Brown, Hannah	Cyna, Allan	Frost, Linda	Hatzirodos, Nicholas	Javadmanesh, Ali	Lee, Susan
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	Dalton, Julia	Fuss, Alexander			Leong, Wai
					Lett, Bron

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